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DEPARTMENT
OF LAW

Personalised Medicine and Patent Law

An Overview of the Patenting of Genetic Inventions
under United States and European Law in Relation
to Genetic Diagnostic Tests

Zeynep Timocin Cantekin

Thesis submitted for assessment with a view to obtaining the degree
of Master in Comparative, European and International Laws (LL.M.)
of the European University Institute

Florence, 30 September 2017

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Thesis Summary

Following the U.S. Supreme Court decisions in *Mayo Collaborative Services v. Prometheus Labs. Inc.* and *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, the future of patentability of genetic material is uncertain. In the U.S., the decision in *Myriad* which allowed the patenting of cDNA molecules seems to have limited the force of the concerned voices from the genomic research community that had called for substantial limitations on the patenting genetic material based on the argument that these patents seriously inhibit genomic research and prevent broader provision of genetic diagnostic tests to the public. In the EU, and in markets under the EPC, the patentability issue remain unclear due to lack of judicial guidance. This *status quo* coincides with the ambitions of governments in both sides of the Atlantic for incentivising research and investment in personalised medicine, a field that is dependent on genetic diagnostic tests and promises radical improvement in public healthcare provision, but also potentially lots of profit and tax. In the light of all these, this paper explores social, political and more particularly legal issues surrounding developments in genomic technologies and personalised medicine, and offers an extensive overview of the limits of substantive patent law in the patenting of genetic inventions in the U.S. and Europe. The paper concludes that the approach of the Biotechnology Directive under EU law setting an over-arching industrial applicability requirement for gene patents offers a balanced response to the challenges created by these patents. Other solutions such as widening the scope of compulsory licensing or the experimental use exception, or creating a *sui generis* gene right are also visited. Finally, new CRISPR technology that might further challenge the existing legal frameworks is briefly introduced.

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A. PERSONALISED MEDICINE, GENETIC DIAGNOSTIC TESTS AND GENE PATENTS

“It’s far more important to know what person the disease has than what disease the person has.”

– Hippocrates¹

“Medicine considers the human body as the means by which it is cured and by which it is driven away from health. The knowledge of anything, since all things have causes, is not acquired or complete unless it is known by its causes. Therefore in medicine we ought to know the causes of sickness and health.”

–Avicenna (On Medicine)²

I. Introduction

Personalised medicine, or precision medicine, in its broadest definition, can be summarised as the practice of medicine tailored to the individual patient. Although the concept is not new, with the recent scientific and technological development of the 21st century, the complete sequencing of the human genome and the rise of genomics, in its most contemporary sense, it means “the delivery of the right drug to the right patient at the right dose.”³ The development of new enabling technologies has made it possible for rapid advancement in the field of personalised medicine in the last two decades. Especially developments in genomics and pharmacogenetics, resulted in an increase in the efficiency of genomic sequencing technology which has made it easier and faster to discover genetic mutations or amplifications⁴ that create disease risk, while enabling cheaper and more accurate genetic tests to search for such risk factors in individual patients.⁵

¹ U.S. Food and Drug Administration (FDA), *Paving the Way for Personalized Medicine: FDA’s Role in a New Era of Medical Product Development* (October 2013), p.5.

² Charles F. Horne (ed.), *The Sacred Books and Early Literature of the East*, Vol. VI: *Medieval Arabia* (Parke, Austin, & Lipscomb, New York 1917), pp.90-91.

³ Alessio Squassina and others, ‘Realities and expectations of pharmacogenomics and personalized medicine: impact of translating genetic knowledge into clinical practice’ (2010) 11(8) *Pharmacogenomics* 1149, p.1150.

⁴ “Gene amplification is an increase in the number of copies of a gene without a proportional increase in other genes. This can result from duplication of a region of DNA that contains a gene through errors in DNA replication and repair machinery as well as through fortuitous capture by selfish genetic elements.” ‘Gene amplification’ in Nature journal website <<https://www.nature.com/subjects/gene-amplification>> accessed 5 August 2017.

⁵ European Parliament, *Personalised medicine: The right treatment for the right person at the right time*, (briefing paper, October 2015), pp.3-4. The cost of gene sequencing has decreased more than 16.000-fold in 10 years since the

Today, our knowledge of the human genome allows us the possibility to develop genetic tests that can diagnose an individual's susceptibility to a certain disease, or provide individual genomic data that helps the clinical practitioner to decide the right treatment and the right dosage, or identify individuals who are unlikely to respond to a certain treatment or drug. All of these properties of personalised medicine place it "on the frontier of healthcare."⁶ Its importance chiefly stems from its implications for public health care: If patients are to receive only the right treatments and drugs that will work best for them, not only the outcomes will significantly improve but also will increase available funds for national healthcare systems as thanks to the personalised medicine applications, national healthcare systems will save money.⁷

Success of personalised medicine enterprises depends on continued efforts in three areas: (1) Knowledge production (research and development); (2) data management⁸; and (3) commercialization (product creation and marketing). Intellectual property law, and especially patent law play a crucial role in all of these areas.⁹ This paper will focus mainly on patent law as a tool to create incentives for personalised medicine research and applications. Before moving on to the outline of this paper, let's explore some additional issues concerning personalised medicine, give a primer on the science involved, and finally demonstrate how gene patents are used to have proprietary control over gene testing applications (which are central to personalised medicine) via an example gene test.

completion of the Human Genome Project (HGP) according to the Personalized Medicine Coalition (PMC). PMC, *The Case for Personalized Medicine* (4th edn 2014), p.4.

⁶ Commission (EC), *European Perspectives in Personalised Medicine*, (conference report: 12-13 May 2011), p.5.

⁷ Ibid.

⁸ Research that leads to clinical applications generally require linking genotype data to phenotype data. This is to reveal the probable expressions of a certain genetic makeup that are clinically significant for a group of patients that will be subject to a personalised medicine intervention. As a result of organization of scientific knowledge production in genomic sciences, several kinds of genotype data and phenotype data are created by different parties with divergent interests; moreover, the different modes that these parties produce data differ in their ability to having the data created protected by intellectual property. It is thus not surprising to observe that governmental initiatives promise legislative action and investment in the area of data management. However it must be kept in mind that if the aim is the increased rollout of new pharmacogenomics products and clinical applications, as the eventual profit from commercialization and leveraging financial risk are crucial concerns for all private parties involved in the effort, the potential for patent protection must be a central issue for any policy. Jasper A. Bovenberg, 'Accessibility of biological data: a role for the European database right?' in David Castle (ed), *The Role of Intellectual Property Rights in Biotechnology Innovation* (Edward Elgar, 2009), p.337.

⁹ Sharon Oriel, 'Making a return on R&D: a business perspective' in David Castle (ed), *The Role of Intellectual Property Rights in Biotechnology Innovation*, (Edward Elgar, 2009), p.131.

II. Personalised Medicine

A personalised medicine application generally consists of two steps that correspond to two separate medical products. The first step is the diagnostic step, where diagnostic methods that include genetic tests, and devices such as imaging equipment, are used to determine the genotype¹⁰ and phenotype¹¹ of the patient. This determination is used to identify the genetic profile of the patient within a subgroup that has been classified previously by research. The second step is the therapeutic stage, where treatment methods and products are used in light of the patient's genetic profile that has been recognized to fall within a subgroup.¹² Therefore, accurate diagnostic methods and in certain cases the determination of particular biomarkers¹³ are critical to the success of personalised medicine applications.¹⁴

Today, modern healthcare provision technique in industrialised nations in great part utilises a trial-and-error method with sub-optimal efficiency whereby therapeutic methods and products are administered to patients based on a medical doctor's diagnosis based on general information.¹⁵ The patient's reaction to the therapeutic method is then observed and in case of unsatisfactory response, the method is changed, e.g. the medications or doses are changed.¹⁶ The personalised medicine concept, on the other hand, envisions wide use of patient stratification based on pharmacogenomics research to forecast drug responses of patients based on their individual characteristics.¹⁷ Once this forecast can be accurately done, the most optimal therapeutic method can be used on the patient, and the waste (in time and money) created by the trial-and-error method can be avoided. This promise of the technology makes development of personalised medicine a politically valuable field for government

¹⁰ Genotype is "the genetic constitution of an organism, as opposed to the expressed features, the phenotype." 'Genotype' in John Lackie (ed), *A Dictionary of Biomedicine* (OUP, 2015 Online Version).

¹¹ Phenotype is "the observable characters, including morphology and behaviour of an organism, regardless of the actual genotype of the organism. Identical genotypes do not necessarily produce identical phenotypes." 'Phenotype' in *ibid*.

¹² FDA, *Paving the Way* (n.1), p.8.

¹³ Biomarker is "an indicator signalling an event or condition in a biological system or sample and giving a measure of exposure, effect, or susceptibility. A biomarker may be a measurable chemical, biochemical, physiological, behavioural, or other alteration within an organism." 'Biomarker' in Richard Cammack and others (eds), *Oxford Dictionary of Biochemistry and Molecular Biology* (2nd edn OUP, 2008 Online Version).

¹⁴ FDA, *Paving the Way* (n.1), p.10.

¹⁵ *Ibid*, p.6.

¹⁶ *Ibid*.

¹⁷ It has been argued certain such stratification in personalised medicine may cause confusing genetic trait based groupings with "sociological" subdivisions such as ethnicity or race and in the process risk misconstruing genetic differences as the 'scientific basis' of such subdivisions, which is a faulty interpretation of the scientific data. Shubha Ghosh, *Identity, Invention, and the Culture of Personalized Medicine Patenting* (CUP, 2012), p.126.

action, as the cost of healthcare services in the private market but also the size of public healthcare expenditures in national budgets is a politically sensitive issue.

Whether personalised medicine as a concept can fulfil these promises is another matter. As advancements in genomic technology make gene testing and genetic research faster and cheaper, the number of genetic variations discovered increases rapidly. It is now known that genetic variations are very common in human beings, even considered by some commentators as the “norm”.¹⁸ Therefore establishing the clinical significance of spotting a variation in an individual for a previously sequenced gene is tricky business. The implications of such high incidence of variation between genomes of individuals for genetic diagnostic based personalised medicine applications are significant. For instance, in a recent article published in the Mosaic science magazine¹⁹ it has been argued that the fact that genetic tests in general yield a high rate of uncertain results as to the pathogenicity causes emotional and psychological distress for patients receiving “unknown significance” results in their genetic tests.²⁰ That article further pointed out that the uncertainty regarding effects of genetic variations and lack of scientific consensus have at least in some instances caused changes in the reported clinical significances of certain variations over time, resulting in lawsuits brought by relatives of patients who got “unknown significance” results in their tests for variations that were upgraded to pathological in the face of more recent scientific findings.²¹ Whether genetic test service providers can be held liable for the confidence of their test results could be a significant legal problem as genetic testing becomes more and more widespread. But also from a healthcare policy perspective (and indeed a philosophical perspective) the idea of a healthcare provision system that comes to depend more frequently on preventative genetic diagnostics and prophylactic measures will pose questions not easy to answer. However, these issues, together with the question of whether personalised medicine research and development, and its clinical applications can provide economic efficiencies that could reflect to healthcare consumers and public budgets as explained above, is not within the scope of this work. Yet, inasmuch as many governments make this case, this paper will be concerned with

¹⁸ “It turns out that rare genetic variants are the norm. We all have hundreds of them. My colleagues and I studied all 20,000 genes in 1,000 random people from the UK general population. We found that, on average, each person had 22,000 variants, of which 160 were very rare, not present in anyone else in the study.” Nazneen Rahman, ‘We need to change the way we think about genetic variation’ (mosaicscience.com, 18 July 2017) <<https://mosaicscience.com/extra/we-need-change-way-we-think-about-genetic-variation>> accessed 18 August 2017.

¹⁹ Published by the Wellcome Trust.

²⁰ Carrie Arnold, ‘The uncertain future of genetic testing’, (mosaicscience.com, 18 July 2017) <<https://mosaicscience.com/story/uncertain-future-genetic-testing>> accessed 18 August 2017.

²¹ Ibid.

finding out the potential of the current patenting landscape for policy goals that seek to create a fertile ground for the development of the personalised medicine technologies.

Although this is not the main focus of this work, a warning must be made against underestimating the complexity of the problems underlying the relatively straightforward sounding policy goal of ‘incentivising the development of a certain field of science or technology’. The economics of the policy notwithstanding, any policy action in the field of science and technology will have to interact with the existing system of scientific production, which has its own complex dynamics. The relationship between science and technical or technological advancement is complex, and cannot be assumed without any critical reflection. The nature of the relationship will and affect the outcomes of any political action aimed at creating technological results for the general public.

Recently, the quality of genomic and other biotechnological research has been subject to much criticism. Daniel Sarewitz, a professor of science and society at Arizona State University, has launched a well publicized criticism of the faulty application of the scientific method in certain scientific areas including biomedical science, claiming that most of the work created in this area is of poor quality and not replicable. He argues that institutions of scientific production nowadays are plagued with a culture that prizes reputation of individual scientists and research institutions that flows from the sheer amount of publications or well-publicised research (and the flow of grant money that corresponds with these) rather than achievement of practical goals, and that the peer-review system of controlling quality of scientific production is failing to weed out bad research due to the vicious synergies of interests that are created by the centrality of reputation. Sarewitz points out to biomedical science as a field particularly affected by this vicious circle²², and argues that the fact that

²² “[...] most of the evidence of poor scientific quality is coming from fields related to health, biomedicine, and psychology [...]”, Daniel Sarewitz, ‘Saving Science’ (Spring/Summer 2016) 49 *The New Atlantis*, pp.4–40; “[...] \$28 billion per year is wasted on biomedical research that is unreproducible. Science isn’t self-correcting; it’s self-destructing.” Leonard P. Freedman and others, ‘The Economics of Reproducibility in Preclinical Research’ (2015) 13-6 *PLOS Biology*, quoted in Sarewitz, ‘Saving Science’. Sarewitz recounts a breast cancer activist Fran Visco’s experience in her struggle to procure funding for breast cancer treatment research: ““all the money that was thrown at breast cancer created more problems than success,” Visco says. What seemed to drive many of the scientists was the desire to “get above the fold on the front page of the New York Times,” not to figure out how to end breast cancer. It seemed to her that creativity was being stifled as researchers displayed “a lemming effect,” chasing abundant research dollars as they rushed from one hot but ultimately fruitless topic to another. “We got tired of seeing so many people build their careers around one gene or one protein,” she says.” Sarewitz, ‘Saving Science’.

biomedical science relies too much on ‘big data’ has made the problem irreproducible and poor results more acute in the field.²³

Certainly, genomic science and genetic engineering, and personalised medicine as a corollary are fields that may be threatened by the developments that Sarewitz warns us. Efforts that supposedly have the goal of nurturing and development of the science and technology of personalised medicine should find solutions to avoid incentivising bad research.

These questions notwithstanding, legal issues surrounding personalised medicine could be said to focus on two broad fields of debate (Box. 1). It can be seen that patent law is closely related most of the problematic topics in these fields.

Moral field: Implications for i) the relationship between personhood and property, ii) the meaning of humanity and the human condition.

Political field: Implications for i) healthcare policy, ii) social policy, and iii) regulation of risk.

Box 1

The first field comprises of disputes that relate to the fundamental philosophical questions surrounding the creation of exclusionary economic rights based on biological processes of the human body, and in a broader context, the moral implications of legal rules that touch issues such as manipulation human nature vis-à-vis a shared humanity. Personalised medicine, by its reliance on gene patents and protections on diagnostic methods, gives rise to these important moral questions that lawyers have to tackle when discussing the appropriate legal framework for this new technological phenomenon. As these moral questions are more likely to be addressed by rational arguments and philosophical discourse, rather than the requirements of political realities such as balancing and compromise, I call this first set of implications ‘moral’, as opposed to political.

The second field comprises of disputes that are related more to the economic and industrial organization that is formed around personalised medicine technology and applications, and accordingly the reflection of this organization on social organizations. In this context, the

²³ Ibid.

legal framework in which personalised medicine proliferates has an effect on the distribution of wealth/welfare and power: Such as how the benefits created by these new applications are distributed amongst the population; how the risk posed by harmful results that might arise from these applications will be managed and the burdens distributed; how the legal protection regime and the revenues that are associated with this protection affects the overall structure of the market for healthcare and the associated industries; or how the new structure of these industries affect the relationship between the actors and regulators in these industries. Having this context in mind, I call the second set of implications ‘political’, in distinction to the first set discussed above.

The problematic area of healthcare policy covers many important questions for policy makers whose answers will to an extent determine the financial landscape of the personalised medicine sector, both in industry and research. The questions are about the incentivising strategies directed to investments in healthcare provision and/or investments in research and development of medical technologies including pharmacogenomics and genetic engineering.

The role of patent law and gene patents in personalised medicine business and policy

Gene patents come in various claim structures, there is no single model.²⁴ Typically the claims are related to two types of inventions; the isolated DNA molecule, and the method for comparing a sample sequence taken from a patient to the claimed reference sequence, and these type of patents might also include claims concerning the drawing of diagnostic conclusions from this comparison.²⁵ Nicholson Price II helpfully groups gene patents relevant to medicine in two categories, namely biotechnological patents and diagnostic patents.²⁶ According to this classification, biotech patents are patents that control the gene sequence encoding a useful protein, thus generating economical value the control over the production that protein product. Diagnostic patents on the other hand seek to control a method for

²⁴ W. Nicholson Price II, ‘Unblocked Future: Why Gene Patents Won’t Hinder Whole Genome Sequencing and Personalized Medicine’, (2012) 33 Cardozo L. Rev. 1601, p.1607.

²⁵ Ibid.

²⁶ Price cites Holman classifying gene patents into four categories, namely biotechnological patents, diagnostic testing, research tools, and forensic testing, but notes that only the first two are “highly relevant” to medicine. Ibid, citing Christopher M. Holman, ‘Trends in Human Gene Patent Litigation’ (2008) 322 Science 198.

determining whether a protein is produced naturally in the patient's body.²⁷ Myriad's BRCA1 patent is a patent of this second type.

This issue of whether gene patents have been stimulating or inhibiting research and development in genomic sciences have been a controversial subject for a long time.²⁸ Concerning the effects of patent law on genetic diagnostic tests, the debate was particularly intense in the U.S. in the second half of 2000s, that is in the period leading to the cases of *Mayo Collaborative Services v. Prometheus Labs. Inc.*²⁹ and *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*³⁰ This period saw vocal expressions of concern from the research community that argued that exclusive licensing practices of university technology transfer offices and industry actors concerning their product and method patents on genes were potentially blocking many new research enterprises, and limiting patient access to genetic tests.³¹ These apprehensions culminated in the preparation of a very critical report by the U.S. Department of Health and Human Services in April 2010 (henceforth SACGHS Patent Report).³²

The SACGHS Patent Report found that (1) “the prospect of patent protection of a genetic research discovery does not play a significant role in motivating scientists to conduct genetic research”, patents had stimulated some private actors into investing in research but since the bulk of the research was funded by the U.S. Government, “patents are not needed for much of U.S. basic genetic research to occur”; also “there is evidence to suggest that patents on genes discourage follow-on research”, “patents are not needed to encourage disclosure in industry”, “no cases [were found] in which possession of exclusive rights was necessary for the development of a particular genetic test”, “exclusive rights do not result in faster test development”, and “patents are already hindering the development of multiplex tests” (2) “Where patents and licensing practices have created a sole provider of a genetic test, patient

²⁷ Price (n.24), p.1608.

²⁸ For a widely cited article that point to the risk of inhibition, see Michael A. Heller and Rebecca S. Eisenberg, ‘Can Patents Deter Innovation? The Anticommons in Biomedical Research’ (1998) 280 Science 698.

²⁹ 132 S. Ct. 1289 (2012).

³⁰ 133 S. Ct. 2107 (2013).

³¹ See generally: Mildred K. Cho and others, ‘Effects of patents and licenses on the provision of clinical genetic testing services’ (2003) 5(1) J Mol Diagnostics 3; K. Jensen and F. Murray, ‘Intellectual property. Enhanced: intellectual property landscape of the human genome’ (2015) 310 Science 239; Timothy Caulfield and others, ‘Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies’ (2006) 24(9) Nature Biotechnology 1091; Robert Cook-Deegan and others, ‘The dangers of diagnostic monopolies’, (2009) 458 Nature 405.

³² U.S. Department of Health and Human Services, *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests: Report of the Secretary's Advisory Committee on Genetics, Health, and Society* [SACGHS Patent Report] (April 2010).

access to those tests has suffered [...]”; and finally (3) “significant concerns about the quality of a genetic test arise when it is provided by a patent-protected sole provider.”³³ The report also made six recommendations, Recommendation 1, which is the most relevant to substantive patent law, recommended:³⁴

“[the promotion of] the following statutory changes:

A. The creation of an exemption from liability for infringement of patent claims on genes for anyone making, using, ordering, offering for sale, or selling a test developed under the patent for patient-care purposes.

B. The creation of an exemption from patent infringement liability for those who use patent-protected genes in the pursuit of research.”³⁵

The SACGHS Patent Report generated a backlash from the industry, academia, and certain scientists equal to it in intensity.³⁶ Some commentators pointed out that the findings of the Report should be interpreted not as failings of the patent system *per se*, but as results of opportunistic and short-sighted patent policy on the part of universities and certain private sector actors.³⁷ It is also argued that the SACGHS findings are mostly relevant to ‘first-generation’ diagnostic tests which were mostly a result of publicly funded genomic research and were highly correlated with disease, whereas next-generation diagnostic tests concerning genetic variations whose correlations to clinical significance are less easily established, require more focused private involvement and investment in order to be developed and marketed.³⁸ For example, in the Myriad case, the SACGHS Report was cited in a negative light by

³³ Ibid, pp.1-4.

³⁴ The findings and recommendations of the Report were not a product of consensus amongst the members of the preparing committee. Three members wrote a joint dissent disagreeing with many of the findings of the report, and *all* the statutory changes that were recommended. They concluded: “The suspension of patent protections such as exemptions from liability for patent infringement for a restricted class of innovation (gene patents), unless they are determined to be non-patentable (for instance, a court determination that they are a “product of nature”), is unwarranted and a risky intrusion in to a process that has delivered many key innovations to needy Americans.” Mara Aspinall and others, ‘Statement of Dissent from Ms. Aspinall, Dr. Billings, and Ms. Walcott’ in SACGHS Patent Report (n.32), in appendix.

³⁵ SACGHS Patent Report (n.32), p.4.

³⁶ See Biotechnology Innovation Organisation (BIO), ‘Hindering Progress: Gene Patent Limits Could Impede Innovation’ (BIO website) <<https://www.bio.org/articles/hindering-progress-gene-patent-limits-could-impede-innovation>> accessed 1 September 2017; Christopher M. Holman, ‘The Critical Role of Patents in the Development, Commercialization and Utilization of Innovative Genetic Diagnostic Tests and Personalized Medicine’ (2015) 21 B.U.J. Sci. & Tech. L. 297, pp.306-312.

³⁷ Julia Carbone and others, ‘DNA patents and Diagnostics: Not a Pretty Picture’ (August 2010) 28(8) Nature Biotechnology 784. For a later work highlighting the role of “practices and institutions” (besides legal rules) in the matter see E. Richard Gold and Julia Carbone, ‘Myriad Genetics: In the eye of the policy storm’ (2010) 12(4 Suppl) Genet Med S39.

³⁸ Holman, ‘The Critical Role of Patents’ (n.36), p.310.

various *amicus curiae* briefs that called for the upholding of gene patents.³⁹ The *amici* brief by Christopher M. Holman and Robert Cook-Deegan in support of neither party pointed out that:

“[...] companies focused on the development of pharmacogenomics and personalized medicine—technologies widely viewed as critical to the future of pharmaceutical development and healthcare—point to gene patents as critical to securing the funding necessary to bring these products to market [...] Affirmance of the decision below [the District Court decision invalidating the claims on genetic material] could dramatically reduce the private incentive for investment in innovation in these and related fields. [...] Much of the future of genetic testing will lie in identifying more complex patterns of genetic variation involving a large number of genes dispersed throughout the genome, or identification of complex gene expression patterns. Personalized medicine will involve identifying correlations between genetic variation and specific therapeutic compounds. These next-generation diagnostic testing products and services might very well require a substantial private investment, increasing the importance of the patent incentive. *A wholesale elimination of patent protection for genetic inventions, as embodied in the decision below, could impair future innovation in diagnostics.*”⁴⁰ [emphasis added]

Today, after the Supreme Court decision in *Myriad* upholding the claim on the cDNA molecule, the debate surrounding the effects of gene patents on the availability of genetic diagnostic tests and their impact on research has subsided somewhat, and the patent system can be said to be still generally considered as a proper incentive for investments in genetic diagnostic tests and their applications.⁴¹

³⁹ Ibid, p.308.

⁴⁰ Christopher M. Holman and Robert Cook-Deegan, ‘Brief of Amici Curiae in Support of Neither Party in *The Association of Molecular Pathology et al. v. USPTO and Myriad Genetics, Inc.*’ (28 Oct 2010) (U.S. Court of Appeals for the Federal Circuit, Docket No. 2010-1406 [653 F.3d 1329]), pp.29-31.

⁴¹ Holman, ‘The Critical Role of Patents’ (n.36), p.308; Leland L. Black, ‘Patenting and Protecting Personalized Medicine Innovation Post-Mayo, *Myriad*, and *Limelight*’ (2017) 95 N.C. L. Rev. 493, pp.493-522.

III. A Primer to the Science Involved⁴²

This section will be helpful in understanding the science described in the later sections in discussing substantive patent law.

The path from DNA to Protein

Proteins are complex molecules that have a crucial role in the structure and activity in every cell and system and thus are essential to the living organism. Proteins consist of one or more amino acid chains (proteins are also called *polypeptides* after the peptide bond that ties the amino acids together) that are folded into different three-dimensional shapes (called “conformations”), which determine their function.⁴³ Proteins vary broadly in size, from 6 to around 33,000 amino acids.⁴⁴

The DNA stores the genetic information required for the synthesis of proteins from amino acids. There are 20 different kinds of amino acids with different chemical properties that are coded for in the DNA. Protein synthesis in a cell happens in two steps called transcription and translation. But before we go into these, I shall briefly explain the structure of the molecules that have a major role in these steps, namely the polynucleotides DNA, RNA and mRNA.

The structure of polynucleotides

The DNA and RNA are polymers that are built from chains of chemical units called nucleotides. This is why they are also called polynucleotides. In a polynucleotide, nucleotides are bounded together in a chain via covalent bonding between the sugar of a nucleotide to the phosphate in the other, to form what is called a sugar-phosphate backbone. Chemically, nucleotides are nitrogenous bases and they are divided into two types according to the structure of their bases; *pyrimidines* and *purines*. The pyrimidine bases in a DNA molecule are

⁴² The scientific background information given in this section follows these two publications: Bruce Alberts and others, *Molecular Biology of the Cell* (6th edn Garland Science, 2015); Neil A. Campbell and others, *Biology: Concepts and Connections* (4th edn Pearson, 2003).

⁴³ Campbell, *Biology* (n.42), p.42. Proteins are divided into seven major classes according to their functions: Structural, contractile (such as in muscular movement), storage, defensive (such as in antibodies), transport (e.g. hemoglobin), signal (e.g. hormones), and enzymes. Enzymes are proteins that catalyse chemical reactions without changing into a different molecule itself; enzymes regulate almost all chemical activity in the organism. Ibid.

⁴⁴ Alberts, *Molecular Biology* (n.42), p.121.

Thymine (T) and Cytosine (C), and the purines are Adenine (A) and Guanine (G). The RNA molecule contains a different pyrimidine Uracil (U), instead of Thymine (T). The chemical properties of the nucleotides make it possible that hydrogen bonds are formed between A bases and T (U in RNA) bases, and between G bases and C bases (in RNA G may occasionally pair with U)⁴⁵. Thus, the pairing nucleotides are said to be “complimentary” to each other.

In nature, the DNA molecule exists in the cell in a structure called the double helix, in which two strands or chains of DNA polynucleotides are attached, or “annealed”, to each other by forming hydrogen bonds between their nucleotides, as explained above. DNA molecules contain the information required for the cell to synthesize proteins (and RNA) as an end product and the double helix structure and the complimentary nature of the nucleotides make it possible for the cell to ‘read’ the code, or genes, contained in the DNA.

Gene and Genome

At this point a short description of the concepts of the gene and the genome could be useful. DNAs of living organisms may contain billions of nucleotides, but only certain specific sequences of nucleotides in any given polynucleotide are significant in the cellular processes of organisms. Such discrete nucleotide sequences in their entirety are called genes. The Oxford Concise Medical Dictionary (9th Ed.) defines gene as:

“the basic unit of genetic material, which is carried at a particular place on a chromosome. Originally it was regarded as the unit of inheritance and mutation but is now usually defined as a sequence of DNA or RNA that acts as the unit controlling the formation of a single polypeptide chain...”⁴⁶

The genome on the other hand signifies the whole set of genes in an organism. The human genome comprises all genes that are located in the 23 chromosome pairs.⁴⁷

⁴⁵ Ibid.

⁴⁶ ‘Gene’ in Elizabeth Martin (ed), *Concise Medical Dictionary* (9th edn OUP, 2015 Online Version).

⁴⁷ ‘Genome’ in *ibid*.

Protein Synthesis

Step 1 in protein synthesis: Transcription and RNA splicing

Transcription is the process of ‘reading’ of a section of the DNA within the cell. Briefly explained, a special protein called the RNA polymerase⁴⁸ breaks open the double helix structure of the DNA, and synthesizes RNA by putting together the nucleotides complimentary to those on the strand of DNA that it is ‘reading’. Thus RNA polymerases ‘transcribe’ the code contained on the DNA onto the RNA molecule.

The RNA polymerase transcribes the target DNA sequence in its entirety on the newly formed RNA. At this point the RNA will include the coding exons but also the non-coding introns in the relevant gene as described above. As the RNA emerges from the RNA polymerase, a process called RNA splicing begins that removes the introns from the new polynucleotide. The chemistry of RNA splicing is complex, and will not be described in detail here. Suffices to say that the resulting molecule that contains only exons is called the mRNA (short for messenger RNA) and abnormal splicing of the RNA may cause diseases and disorders. The production of the mRNA brings us to the next step in the path from DNA to protein: translation.

As a caveat, we should add that for many genes, the end product is not a protein but RNA molecules with specialised functions. There are various chemical activities in the cell in which specialised RNA have a role, such as in RNA splicing or translation.⁴⁹

Complimentary DNA (cDNA)

Before moving on to the second step in protein synthesis in the cell, we should stop to introduce an important concept for patent law and genomics research and industry in general. As explained above, the mature mRNA as produced in the nucleus of the eukaryotic cell contains information in a structure required for protein synthesis in a cell, that is, a gene sequence comprised of only exons that will correspond to a protein when processed by the

⁴⁸ While bacteria only have one type of RNA polymerase, there are three types of RNA polymerases in eukaryotic cells (types I, II and III). In eukaryotes, protein-coding genes are transcribed by RNA polymerase II. Alberts, *Molecular Biology* (n.42), p.309.

⁴⁹ Ibid, p.333.

ribosomes of a competent cell. Simplified, the mRNA is the recipe for a protein written in the alphabet of the four nucleotides. However the mRNA as a molecule is not useful by itself for genetic engineering purposes. So methods have been developed to transcribe the information coded in the mRNA to a single stranded DNA polynucleotide, which can be later used in applications such as cloning the gene in bacteria or introducing the DNA in another organism to express proteins.⁵⁰

The polynucleotide synthesised by transcription from an mRNA is called complimentary DNA, or cDNA. The production of the cDNA conceptually plays a crucial role in patent law, as the creation of the cDNA under laboratory conditions and with human interference makes it an important point for arguments concerning patentability that cDNA is different from the naturally occurring molecule, given that the invention being not naturally occurring is essential for patent-eligibility under the patent laws of many jurisdictions.⁵¹ The fact that the same DNA sequence can be spliced in different ways in the cell to produce mRNAs coding for varying proteins⁵² is another reason that makes cDNA important element in protecting protein products by patents.

Step 2 in protein synthesis: Translation

Once a mature mRNA molecule is formed, the next step in the path from DNA to protein is the conversion of the information encoded in the mRNA in the language of the four nucleotides into a recipe that instructs which and how many of the 20 amino acids will be assembled to build the polypeptide; thus the term ‘translation’. In this step, specialised RNA molecules called transfer RNA, or tRNA, couple with amino acids that correspond to their individual specific chemical attributes. Then, within a molecular structure called a ribosome, the tRNA molecule attaches its zone called the *anticodon* to three consecutive nucleotides on the mRNA strand, called collectively a *codon*. Once attached to the codon, the tRNA adds the amino acid it has coupled with to the end of the amino acid that a previous tRNA attached to the previous codon had brought into the ribosome, forming a polypeptide chain, which after completion folds into a protein or a subunit of a protein.

⁵⁰ Ibid.

⁵¹ *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.* 133 S. Ct. 2107 (2013).

⁵² Alberts, *Molecular Biology* (n.42), p.319.

This ordered placement of amino acids in a polypeptide chain in accordance with the consecutive three-nucleotide codons in the mRNA sequence is the essence of what is called the “genetic code”. The rules of the genetic code were deciphered in the 1960s, which signified a breakthrough in genomic science. Most amino acids are coded by more than one codon, while some are coded by only one.⁵³ One codon also acts as a signal for the beginning of the protein-coding sequence, and three distinct codons represent the end of the sequence.⁵⁴

IV. An Example Gene Test with Commentary

The following example gene test (‘assay’) was given the patent description of Myriad Genetics, Inc.’s BRCA1 patent⁵⁵ that was at issue in the U.S. Supreme Court case of *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*⁵⁶ The fragments in bold italics are the original text of the example gene test. Text in square brackets is my commentary. Underlined text highlights the points where the patent interferes with the method. The numbered claims refer to the claims of the BRCA1 patent.⁵⁷ The purpose of this section is to explain how gene patents can provide to right holders exclusionary proprietary control over gene test applications. This gene test is a basic test using somewhat old technology, but the method is still relevant and easy to follow and explain.

⁵³ For example, the codon UGG codes only for the amino acid Trp (Tryptophan) while Ala (Alanine) is coded by GCA, GCC, GCG, or GCU (Note that uracil (U) corresponds to thymine (T) in DNA). Ibid, p.334. To provide an actual example, in Myriad’s BRCA1 patent (U.S. Pat. No 5,747,282) claim 1 claims the DNA sequence coding for a BRCA1 polypeptide with the sequence MetAspLeuSerAlaLeu(...), the reader may compare this sequence to the DNA sequence claimed in claim 2 and find that the polypeptide sequence corresponds to the DNA sequence starting from nucleotide position 120: ATGGATTATCTGCTCTT(...) The first 119 nucleotides are not translated in protein synthesis. Such untranslated sequences at the beginning of the coding region of the gene exist in all mRNAs and have various functions including the regulation of the translation process. They are collectively called the 5’ untranslated region, or 5’UTR. Sandrine Caputo and others, ‘Description and analysis of genetic variants in French hereditary breast and ovarian cancer families recorded in the UMD-BRCA1/BRCA2 databases’ (2012) 40 Nucleic Acids Research, pp.D992-D1002; Emanuela Signori and others, ‘A somatic mutation in the 5’UTR of BRCA1 gene in sporadic breast cancer causes down-modulation of translation efficiency’ (2001) 20 Oncogene 4596. See BRCA1 mRNA GenBank database entry: M.H. Skolnick, ‘Homo sapiens breast and ovarian cancer susceptibility (BRCA1) mRNA, complete cds’ <<https://www.ncbi.nlm.nih.gov/nuccore/U14680>> accessed 20 August 2017.

⁵⁴ The AUG codon acts both as the “initiation codon” but also codes for Met (Methionine), while UAA, UAG and UGA act as ‘STOP’ codons. Alberts, *Molecular Biology* (n.42), p.319.

⁵⁵ Myriad Genetics, Inc. (1998) ‘17Q-linked breast and ovarian cancer susceptibility gene’ (U.S. Patent No: 5,747,282).

⁵⁶ 133 S. Ct. 2107 (2013). The case will be examined in detail in Part B below.

⁵⁷ Text of the claims are not provided here for brevity. See patent text (n.55) at <<https://patents.google.com/patent/US5747282A/en>>

EXAMPLE 11 Two Step Assay to Detect the Presence of BRCA1 in a Sample

Patient sample is processed according to the method disclosed by Antonarakis et al. (1985), separated through a 1% agarose gel and transferred to nylon membrane for Southern blot analysis.

[*ZTC: “Antonarakis et al...” Example uses of the invention proposed in the patent are based on previously discovered methods to prove industrial applicability of the invention. Here the DNA sample taken from the patient is isolated and cloned by the cited method, and the cloned patient sample DNA is then transferred to a membrane on which the test is going to be made.^{58]}

Membranes are UV cross linked at 150 mJ using a GS Gene Linker (Bio-Rad). BRCA1 probe corresponding to nucleotide positions 3631-3930 of SEQ ID NO:1 is subcloned into pTZ18U.

[*ZTC: Here the patient sample DNA on the membrane are immobilized by a technique called UV crosslinking. Then, a BRCA1 probe is cloned.⁵⁹ Cloning is done by first combining the gene of interest (BRCA1) into the commercially available cloning phagemid pTZ18U. The phagemid is a “vector”, or a small DNA molecule that is used for introducing a recombinant gene into a bacterium. The gene will then replicate itself using the organism of the bacterium, multiplying the amount of the sample DNA. Note that first clause of Claim 8 covers the phagemid in which the BRCA1 gene is combined (“a replicative cloning vector”), and the second clause covers the DNA that are created by the self replication of the phagemid in the bacterium (“a replicon operative in a host cell.”) The “subcloning” of the BRCA1 probes into the phagemid is achieved by first cutting out the desired length of BRCA1 gene from BRCA1 samples amplified by techniques such as polymerase chain reaction (PCR) and

⁵⁸ S. E. Antonarakis and others, ‘Hemophilia A Detection of Molecular Defects and of Carriers by DNA Analysis’ (1985) 313 N Engl J Med 842. The method uses the technique of “Southern blotting”. Blotting is “a general term for transferring molecules from an acrylamide or agarose gel in which they have been separated electrophoretically, to a paper-like membrane, usually nylon or nitrocellulose, maintaining the spatial arrangement. The binding interaction with the membrane can then be stabilized and the bound molecules can be detected at high sensitivity by hybridization (in the case of DNA and RNA), or antibody labelling (in the case of protein). RNA blots are called *northern blots*, DNA blots are *Southern blots*, (named after E. Southern, who developed the technique), protein blots are *western blots*. In *northwestern blotting* protein is transferred but is probed with specific RNA[...]”. ‘Blotting’ in Lackie, *A Dictionary of Biomedicine* (n.10).

⁵⁹ Probe is: “(in molecular biology), a shorthand term for a labelled complementary sequence of DNA or RNA that will hybridize with the relevant sequence in a test sample. The label chosen depends on the detection system to be employed (e.g. radioactive or fluorescent labels).” ‘Probe’ in *ibid*. ‘Hybridization’ and the use of probes are discussed in length below in the text.

recombining them into the phagemid. Note that Claims 16 and 17 cover the “prime” molecules required to start the PCR process to produce a viable amount of sample BRCA1 genes.⁶⁰ Also Claim 18 covers detection kits that include at least one ‘prime’ molecule.]

The phagemids are transformed into E. coli MV1190 infected with M13KO7 helper phage (Bio-Rad, Richmond, Calif.). Single stranded DNA is isolated according to standard procedures (see Sambrook et al., 1989).

[*ZTC: Then this phagemid is placed into E. coli bacteria of strain MV1190, which in combination with the M13KO7 ‘helper’ virus that are made to infect the bacteria, synthesize and secrete single stranded copies of the DNA contained by the phagemid. This single stranded DNA that are copied in the E. coli are then isolated using a chemical process.⁶¹ This isolated single stranded DNA (vector DNA) will be used as the primary probe in the hybridization process described below. Note that Claim 2, 3 and 5 cover the probe molecule. Claim 7 covers different variants of the gene of interest that may also be cloned as probes and used in the test.

“...phagemids are transformed into E. coli...”: The “scope note” accompanying the entry for “***Transformation, Bacterial***” in the U.S. National Library of Medicine Medical Subjects Headings list (MeSH) states: “The heritable modification of the properties of a competent bacterium by naked DNA from another source. The uptake of naked DNA is a naturally occurring phenomenon in some bacteria. It is often used as a gene transfer technique”.^{62]}

⁶⁰ From the text of the patent description (n.55): “The primer pairs of the present invention are useful for determination of the nucleotide sequence of a particular BRCA1 allele using PCR. The pairs of single-stranded DNA primers can be annealed to sequences within or surrounding the BRCA1 gene on chromosome 17q21 in order to prime amplifying DNA synthesis of the BRCA1 gene itself. A complete set of these primers allows synthesis of all of the nucleotides of the BRCA1 gene coding sequences, i.e., the exons. The set of primers preferably allows synthesis of both intron and exon sequences. Allele-specific primers can also be used. Such primers anneal only to particular BRCA1 mutant alleles, and thus will only amplify a product in the presence of the mutant allele as a template.”

⁶¹ For detailed description (or “recipe”) of the cloning process see Joseph Sambrook and others, *Molecular Cloning: A Laboratory Manual* (Cold Spring Harbor Laboratory Press, 2000), Chapter 3 Protocols 6-8. For phagemid vector cloning with helper phages see Marjorie A. Hoy, *Insect Molecular Genetics: An Introduction to Principles and Applications*, (Academic Press, 1994), p.168; Antibody Design Laboratories, ‘Working with helper phages’ <<http://abdesignlabs.com/technical-resources/helper-phages/>> accessed 10 August 2017.

⁶² U.S. National Library of Medicine, ‘Transformation, Bacterial MeSH Descriptor Data 2017’, <<https://meshb.nlm.nih.gov/record/ui?name=TRANSFORMATION,%20BACTERIAL>> accessed 10 August 2017.

Blots are prehybridized for 15-30 min at 65° C. in 7% sodium dodecyl sulfate (SDS) in 0.5M NaPO₄. The methods follow those described by Nguyen et al., 1992. The blots are hybridized overnight at 65° C. in 7% SDS, 0.5M NaPO₄ with 25-50 ng/ml single stranded probe DNA. Post-hybridization washes consist of two 30 min washes in 5% SDS, 40 mM NaPO₄ at 65° C., followed by two 30 min washes in 1% SDS, 40 mM NaPO₄ at 65° C.

[*ZTC: Hybridization is the process used to test whether a sample polynucleotide contains a certain gene of interest. This is done by introducing single stranded sample polynucleotides and single stranded reference polynucleotides containing the gene of interest to the same medium. If the sample polynucleotide contains the gene of interest, the reference polynucleotide, called a hybridization probe, will ‘anneal’ to it, creating a double stranded molecule as the corresponding nucleotides of the sample and probe will correspond and form hydrogen bonds. The reference polynucleotide, or probe, is attached with a molecular marker, or ‘label’; that is a molecule that is capable to be detected by various methods. For example, a reference polynucleotide may be attached with a radioactive molecule that can be easily spotted by various imaging methods such as autoradiography. These probes are called radiolabeled probes. Labels can also be non-radioactive. In this test, a non-radioactive chemiluminescent marker, AMPPD, is used together with an alkaline-phosphatase labels that activates the marker. When an AMPPD substrate is added to the medium containing probes attached with alkaline-phosphatase labels, the labels activate the AMPPD, and the probes will show up on X-ray film.

This test is a two-step assay, in which two hybridization procedures are run on the patient sample DNA. In the first step, vector DNA containing the primary probe are hybridized with the patient sample DNA. Recall that the primary probe contains the gene of interest, namely the BRCA1. The primary probe will anneal with a patient sample DNA if that DNA contains the gene of interest. In the second step, a secondary probe is hybridized with the vector DNA. The primary probes are not labeled. The secondary probe is a commercially available oligonucleotide probe that has an alkaline-phosphatase label. During the second-step this secondary probe anneals to a separate section of the vector DNA. The technical result is that the signal to noise ratio becomes higher, but since the second probe attaches to the single stranded phagemid DNA containing the gene of interest that has already annealed to the patient sample (if test is positive) detection of the second probe label

in imaging means that the primary probe has successfully hybridized, therefore a positive result.^{63]}

Next the blots are rinsed with phosphate buffered saline (pH 6.8) for 5 min at room temperature and incubated with 0.2% casein in PBS for 30-60 min at room temperature and rinsed in PBS for 5 min. The blots are then preincubated for 5-10 minutes in a shaking water bath at 45° C. with hybridization buffer consisting of 6M urea, 0.3M NaCl, and 5X Denhardt's solution (see Sambrook, et al., 1989). The buffer is removed and replaced with 50-75 µl/cm² fresh hybridization buffer plus 2.5 nM of the covalently cross-linked oligonucleotide-alkaline phosphatase conjugate with the nucleotide sequence complementary to the universal primer site (UP-AP, Bio-Rad). The blots are hybridized for 20-30 min at 45° C. and post hybridization washes are incubated at 45° C. as two 10 min washes in 6M urea, 1× standard saline citrate (SSC), 0.1% SDS and one 10 min wash in 1× SSC, 0.1% Triton®X-100. The blots are rinsed for 10 min at room temperature with 1× SSC.

[*ZTC: This is the second-step hybridization mentioned in the above comment.]

Blots are incubated for 10 min at room temperature with shaking in the substrate buffer consisting of 0.1M diethanolamine, 1 mM MgCl₂, 0.02% sodium azide, pH 10.0. Individual blots are placed in heat sealable bags with substrate buffer and 0.2 mM AMPPD (3-(2'-spiroadamantane)-4-methoxy -4-(3'-phosphoryloxy)phenyl-1,2-dioxetane, disodium salt, Bio-Rad). After a 20 min incubation at room temperature with shaking, the excess AMPPD solution is removed. The blot is exposed to X-ray film overnight. Positive bands indicate the presence of BRCA1.

[*ZTC: As described in my comment above, the AMPPD solution that is added to the blot will be activated by the labels attached to the secondary probes that have annealed with the vector DNA. The blot will contain meaningful amounts of the vector DNA (thus also secondary probes) only if the patient sample DNA immobilized in the medium also contains the gene of interest that the primary probe would have annealed to. Thus, positive bands on the X-ray film means that the patient sample DNA contains BRCA1. Note that while various

⁶³ Annette Tumolo and others, 'Detection of DNA on Membranes with Alkaline Phosphatase-Labeled Probes and Chemiluminescent CSPD Substrate' in Larry J. Kricka (ed), *Nonisotopic Probing, Blotting, and Sequencing* (2nd edn Academic Press, 1995), p.154 et seq.

stages of this test are controlled by claims over individual molecules, if it were combined to be commercialized as a product (a kit), the overall test would be covered by Claim 19.]

After establishing the centrality of gene patents in genetic diagnostic tests, let's move on to the scope of this paper and what will be discussed in the following sections.

V. Outline of This Paper

This paper will explore the limits of substantive patent law in addressing gene patents, focusing specifically on how the European substantive patent law under the European Patent Convention and the Biotechnology Directive under the EU law deals with the patentability of genetic sequences. As the evolution of patent law in dealing with gene patents stems from the patent law's treatment of biotechnological inventions before finally reaching genetic sequences, some portion of the paper will deal with patentability of biotechnological inventions in general. The goal of this paper is to trace the evolution of the interpretations of the definitions of substantive patentability requirements of patentable subject matter, novelty, inventive step, industrial applicability and sufficiency of disclosure in the case law in the boards of the European Patent Organisation and of the European Court of Justice with regards to patents on biotechnological inventions and specifically concerning genetic material.

The result of this inquiry aims to demonstrate the potential the European Patent Convention and the Biotechnology Directive under the EU law in dealing with the gene patents that are important for the viability of personalised medicine, which is largely based on genetic diagnostic tests. In this quest, the paper aims to answer the following questions: (1) What objective does the law try to achieve in the design of the European patent law? (2) How has the law evolved since the 1980s in dealing with the biotechnological inventions i.e. gene patents? (3) After the gene patent challenge, does the design of the law achieve its desired impact? (4) What are the shortcomings of the European Patent Convention with regards to gene patents? (5) After the enactment of the Biotechnology Directive, what are the implications of the way the European Patent Office and the European Court of Justice is willing to treat gene patents for the future of genetic inventions? My hope is that this paper will serve to contribute to the literature by providing a text where the reader can find the state of the art in the legal field concerning gene patents, but also presenting an overview (in detail

that surpasses what is found in most legal contributions) of how exactly these legal rules interact with the science and technical developments that underlie the development of new advanced healthcare applications that we have started to encounter in our daily lives.

To achieve the stated aim, in Part A, an account of the concept of personalised medicine was given, and the issues surrounding the concept and political action whose goal is to incentivise its development was demonstrated. A primer on the scientific background was given for the convenience of the reader who is not familiar with the relevant concepts. Finally, the centrality of gene patents to proprietary control over genetic diagnostic tests was showed by way of an example gene test. Part B focuses on the relevant scientific and technological developments that gave rise to inventions that have challenged the substantive patent laws and more specifically how the U.S. patent law responded to these challenges. First, an account of biotechnology and biotechnological inventions are given. After establishing the importance of U.S. patent law for a Europe focused paper, a primer on U.S. patent law is given, and then the evolution of the relevant turning points in science are discussed alongside with the most relevant landmark cases in the U.S.. Part C focuses on how the substantive European patent law under the European Patent Convention and the Biotechnology Directive responds to the challenges posed by gene patents. After discussing the history and justifications for patent law, first the substantive patentability requirements concerning gene patents under the European Patent Convention will be discussed, and finally the overarching concept of industrial applicability under the Biotechnology Directive will be examined. The final Part D will conclude this paper by briefly looking at options (other than the overarching concept of industrial applicability under the Biotechnology Directive) of a compulsory licensing, a broader experimental use exception, and a potential *sui generis* gene right that might be useful in preventing issues resulting from gene patents that was discussed in Part C. Finally, I will conclude this paper by providing an introduction into the new CRISPR technology that might further challenge the existing legal frameworks.

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B. HISTORY OF PATENTING GENETIC MATERIAL AND THE U.S. EXPERIENCE

I. Introduction: General Starting Points

Biotechnology is “any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.”⁶⁴ The development of biotechnology can be divided into two periods⁶⁵: (1) “Traditional biotechnology”, when applied biology was used to produce food, cultivate plants and dispose waste⁶⁶; and (2) “innovative or advanced biotechnology”, which starts with the discovery of the structure of the DNA in 1953⁶⁷ and later followed by the advance of genetic engineering.⁶⁸ As our understanding of biology expands, biotechnology too continues to evolve. Today, with new CRISPR technology⁶⁹, we might witness the beginning of a third period.

Biotechnology is very important for the health sector. Currently, most of biotechnological research is for the development of personalised medicine rather than development of new drugs.⁷⁰ As introduced in the previous part, for the development of personalised medicine, securing gene patents are important for the sustainability of the industry.⁷¹ A ‘gene patent’ can be described as a patent claiming “a specific and isolated genetic sequence, its chemical composition, the process used to obtain or use it, or combination of these.”⁷² The demand by the industry for developing personalised medicine applications, further complicated the way patent law (national, regional, and international) deals with gene patents. The increased demand for gene patents intensified these complexities, which can be summarised under two headings: (1) Are biotechnological inventions, and more specifically gene patents for the purposes of this paper, patent eligible under current substantive patentability requirements?; and (2) is it ethical to patent genetic material?

⁶⁴ United Nations Convention on Biological Diversity, 5 June 1992, 31 ILM 818, Article 2.

⁶⁵ Andrea Stazi, *Biotechnological Inventions and Patentability of Life. The US and European Experience*. (Edward Elgar, 2015), p.2.

⁶⁶ Ibid.

⁶⁷ James D. Watson and Francis H. Crick, ‘A Structure for Deoxyribose Nucleic Acid’ (1953) 171 Nature 737.

⁶⁸ Stazi (n.65), p.2.

⁶⁹ See section titled ‘CRISPR and the Future’ in Part D below.

⁷⁰ Stazi (n.65), p.8.

⁷¹ See example gene test in Part A above.

⁷² Stazi (n.65), p.6.

Although the main focus of this paper is the European response to these legal complexities concerning gene patents⁷³, it is important to also consider how the U.S. has responded to the challenge posed by the gene patents. This is because in order for Europe to compete with the U.S. (and also with its other major trading partners) at the global level, it is important to have equivalent protection granted to such inventions.⁷⁴ It is also important to note that the U.S. is the cradle of the biotechnological industry. Therefore, before continuing on to the European substantive patent law in the following part, I will briefly introduce the major turning points in history, both legally and scientifically, in the following sections. But first, let's move on to a very brief introduction to U.S. patent law, as this primer will be helpful in explaining the major landmark cases in the U.S., which eventually resulted in the patenting of genetic material both in the U.S. and in Europe.

II. A Primer to U.S. Patent Law

The U.S. Patent and Trademark Office (henceforth USPTO) reviews duly filed patent applications by assessing whether they have fulfilled five requirements. These requirements are patentable subject matter⁷⁵, utility⁷⁶, novelty⁷⁷, non-obviousness⁷⁸ and disclosure⁷⁹. For the purposes of this section and the later comparison with the European industrial applicability requirement in the following part, the remaining substantive patent law requirements of novelty, non-obviousness and disclosure/enableness stay outside the scope of this section.

i) Eligibility, or Patentable Subject Matter

The invention for which patent protection is sought must fall under patentable subject matter as set forth in Section 101 of the U.S. Code Title 35, which stipulates:

⁷³ See Part C below.

⁷⁴ Stazi (n.65), pp.17-18.

⁷⁵ 35 U.S.C. §101.

⁷⁶ Ibid.

⁷⁷ 35 U.S.C. §102.

⁷⁸ 35 U.S.C. §103.

⁷⁹ 35 U.S.C. §112.

“Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.”

Although the scope of patentable subject matter under U.S. law has historically varied due to the changing jurisprudence of courts and the evolution of dominant positions in Anglo-American intellectual property law theory, the development in the law that took place beginning in the 1980s is the most relevant for the subject of this paper.⁸⁰

In early 1980s, the way already opened by Supreme Court’s (henceforth SCOTUS) *Diamond v. Chakrabarty*⁸¹ decision in 1980, and abandoning former patent eligibility doctrines, the Court of Appeals for the Federal Circuit (henceforth CAFC) relaxed the scope of patent protection considerably.^{82,83} The SCOTUS did not rule on the matter of patentable subject matter in the period between 1981-2010, until the liberal ‘anything-under-the-sun’ eligibility regime was somewhat limited by the SCOTUS decisions in *Bilski v. Kappos*⁸⁴; *Mayo Collaborative Services v. Prometheus Labs. Inc.*⁸⁵; *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*⁸⁶; and *Alice Corp. v. CLS Bank Int’l*^{87, 88}

Generally, courts have treated the eligibility requirement as a preliminary condition, rather than a full-fledged substantive test, for an invention to be considered for patent protection.⁸⁹ The eligibility requirement and its conceptualisation as a preliminary condition have had important implications for biotechnological inventions. The prohibition against granting patent protection for ‘products of nature’ finds its basis in the eligibility condition, and whether this condition should be considered as a broad preliminary ‘entry test’ to the patent

⁸⁰ Mark A. Lemley, Peter S. Menell, Robert P. Merges, *Intellectual Property in the Technological Age* (Vol.1 Clause 8 Publishing, 2016), pp.III-123-128.

⁸¹ 447 U.S. 303 (1980).

⁸² Lemley (n.80), pp.III-123-128.

⁸³ See the following section 3(9)(a) below on *Diamond v. Chakrabarty*.

⁸⁴ 561 U.S. 593 (2010).

⁸⁵ 132 S. Ct. 1289 (2012).

⁸⁶ 133 S. Ct. 2107 (2013).

⁸⁷ 134 S. Ct. 2347 (2014).

⁸⁸ Lemley (n.80), p.III-123. Also recently the scope of patentable subject matter has been limited with statute for the first time in U.S. history with the Leahy-Smith America Invents Act (AIA) which expressly prohibits patents on tax strategies and human organisms. Ibid.

⁸⁹ Philippe G. Ducor, *Patenting the Recombinant Products of Biotechnology and Other Molecules*, (Kluwer Law International, 1998), p.6.

system, or a more substantial test in its own right has been a critical issue in the debate surrounding the permissible width of gene patent claims under U.S. patent law. Under U.S. patent law, the prohibition against the protection of products of nature essentially requires an intervention to be done to the natural state of the subject matter of the claim for the claim to be patent eligible. In one of the early precedents on patentable subject matter and the product of nature doctrine, the court held in the *Funk Bros. Seed Co. v. Kalo Co.*⁹⁰ that:

“[...] patents cannot issue for the discovery of the phenomena of nature. [...] The qualities of these bacteria, like the heat of sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none. He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end’.”⁹¹

From this requirement for an intervention stems the importance of isolation and purification of organic molecules in the context of genetic and chemical patents.⁹²

ii) Utility

The utility requirement in Section 101 (“any new and *useful* process”) is currently framed by the SCOTUS decision in *Brenner v. Manson*⁹³, and the subsequent CAFC decision in *in re Brana*.⁹⁴ The SCOTUS decision in *Brenner v. Manson* was a reaction to the Court of Customs and Patent Appeals (henceforth CCPA)⁹⁵ decisions in *in re Manson*,⁹⁶ and the earlier *in re Nelson*⁹⁷ which virtually rejected an autonomous utility test in the patentability assessment.⁹⁸

⁹⁰ 333 U.S. 127 (1948)

⁹¹ *Ibid* at 130.

⁹² *Ducor* (n.89), p.6.

⁹³ 383 U.S. 519 (1966).

⁹⁴ 51 F.3d 1560 (Fed. Cir. 1995).

⁹⁵ The CCPA (Court of Customs and Patent Appeals) was a U.S. federal court that had jurisdiction over appeals from the Patent Office in patent and trademark cases. The CCPA was abolished in 1982 and its duties were taken over by the U.S. Court of Appeals for the Federal Circuit. Federal Judicial Center (FJC) ‘U.S. Court of Customs and Patent Appeals, 1929-1982’ (FJC Website) <<https://www.fjc.gov/history/courts/u.s.-court-customs-and-patent-appeals-1929-1982>> accessed 1 September 2017.

⁹⁶ 333 F.2d 234 (CCPA 1964).

⁹⁷ 280 F.2d 172 (CCPA 1960).

⁹⁸ *Ducor* (n.89), p.7.

In *Brenner v. Manson*, Manson's patent application covered a novel method to produce a chemical compound which itself did not have a precise known use, but whose chemical homologues were deliberated in scientific literature to have potential uses. The SCOTUS ruled that the utility requirement for a chemical process is not satisfied by merely showing that serious research and investigation were being conducted for potential use, and that chemical processes do not fulfil the utility requirement by virtue of the fact that they yield the intended end product.⁹⁹

The strict retrenchment of the utility requirement that came about with the SCOTUS decision was moderated in the context of pharmaceuticals in the following CCPA decisions that allowed lower thresholds for demonstrating utility; in the 1970s, after the SCOTUS decision, animal testing was deemed sufficient to assert use in humans, progressively *in vitro* assays instead of *in vivo* testing in animals were allowed as proof of utility.¹⁰⁰ In the 1980s, the CCPA decision in *Nelson v. Bowler*¹⁰¹ and the CAFC decision in *Cross v. Iizuka*¹⁰² effectively eliminated the animal experiment requirement by allowing the demonstration of any pharmaceutical activity to be sufficient proof of utility, rendering (respectively) the demonstration of pharmaceutical effect on an isolated tissue, and the mere *in vitro* demonstration of enzymatic inhibition sufficient to prove utility.¹⁰³ In light of the *Nelson v. Bowler* and *Cross v. Iizuka* decisions, the Manual of Patent Examining Procedures of the USPTO was updated to reflect the new standard, however despite this change and supporting court decisions many USPTO examiners kept applying an excessively strict utility test, including in the field of biotechnology.¹⁰⁴ This led to the CAFC decision *in re Brana* that reversed a USPTO Board decision by asserting the standard set by the two former decisions, and prompted an update of the USPTO Utility Examination Guidelines in 1995 following the CAFC's calls for caution and evidence from public hearings.¹⁰⁵ However, in light of public comments that suggested that the revised guidelines allowed examiners grant patents

⁹⁹ *Brenner v. Manson* (n.93). The Court found that: "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point -- where specific benefit exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Ibid at 534-535.

¹⁰⁰ Ducor (n.89), pp.8-9.

¹⁰¹ 626 F.2d 853 (CCPA 1980).

¹⁰² *Cross v. Iizuka* 753 F.2d 1040 (Fed. Cir. 1985).

¹⁰³ Ibid.

¹⁰⁴ Ducor (n.89), p.10.

¹⁰⁵ Ibid; Kshitij Kumar Singh, *Biotechnology and Intellectual Property Rights: Legal and Social Implications* (Springer, 2015), p.56.

with unspecific or unsubstantial utility, the Guidelines were further updated in 2000 (entered into force in 2001), adding an additional ‘substantial utility’ requirement to remedy the situation.¹⁰⁶ In 2005, the CAFC approved the final version of the revised USPTO Guidelines in *in re Fisher*.¹⁰⁷ Finally in 2014, the USPTO issued a guidance on the patent eligibility of genes after the SCOTUS decision in *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.* (2013) (superseding an earlier memorandum also concerning *Myriad*).¹⁰⁸

Now let's move on to the history of patenting genetic material and the evolution of the relationship between the U.S. patent law through U.S. landmark decisions.

III. History of Gene Patenting: The Turning Points¹⁰⁹

The advent of two new technologies in the second half of the 20th century, i.e. the discovery of the double helix of DNA and the invention of semiconductor chips, gave rise to inventions concerning biotechnology and computer science.¹¹⁰ The rules and doctrines of patent laws in the U.S. and Europe were challenged by these new technologies with regard to their ability to grant patents to such new inventions. Moreover, as new industries stemmed from these new technologies, and these new industries became the new driving forces in the national and global economies, patent applications of such new inventions grew proportionately.¹¹¹ For example, since the mid-20th century, the advancing knowledge in molecular biology created two new industries, i.e. biotechnology and pharmaceuticals.¹¹² According to Sherkow and Greely, “these industrial developments could not exist without supporting legal structures.”¹¹³

Without new guidance explicitly addressing these new inventions, the patent offices continued to apply the existing rules and doctrines in a flexible way to accommodate the patentability of these new inventions. This gave rise to debate on whether patent law rules and doctrines

¹⁰⁶ Marta Diaz Pozo, *Patenting Genes: The Requirement of Industrial Application*, (Edward Elgar, 2017), p.46.

¹⁰⁷ 421 F.3d 1365 (Fed. Cir. 2005).

¹⁰⁸ Tug Ingram, ‘Association for Molecular Pathology v. Myriad Genetics, Inc.: The Product of Nature Doctrine Revisited’ (2014) 29 Berkeley Tech. L.J. 385, pp.414-415.

¹⁰⁹ For a more detailed overview see, Luigi Palombi, *Gene Cartels: Biotech Patents in the Age of Free Trade*, (Edward Elgar, 2009), pp.226-274.

¹¹⁰ Hugh B. Wellons and others, *Biotechnology and the Law* (American Bar Association, 2007), p.2.

¹¹¹ Jacob Sherkow and Henry Greely, ‘The History of Patenting Genetic Material’ (2015) 49 Annual Review of Genetics 161, p.161.

¹¹² Ibid, p.162.

¹¹³ Ibid, p.161.

should apply differently to different technologies.¹¹⁴ Nonetheless, broader interpretations of the existing patent laws caused public and legal debate. Patentability of these inventions were challenged under two main questions: (1) Are they patent-eligible under the current patent laws and doctrines?¹¹⁵ (2) Are they patent-worthy?¹¹⁶ Inventions stemming from biotechnology have been given the most exceptions in terms of patentability because it has long been argued by the biotechnology industry that otherwise they would not be able to mitigate the financial risks associated with biotechnological research and development, sustain their businesses, and continue investing.¹¹⁷

For the purposes of this paper, among all the biotechnological inventions, our focus will be on the patentability of claims concerning the composition of isolated genes and process claims that are based on defined sequences, which are central to personalised medicine applications based on genetic testing. The centrality of these types of claims is demonstrated in the previous part.¹¹⁸ Moreover, for the purposes of this section, we will focus on the evolution of the patentability of genes under the U.S. patent law, before we move on to the European response to gene patents in the next part. The debate on the patentability of genetic sequences seems to be resolved in the U.S. after the SCOTUS ruling in the case of *Ass'n for Molecular Pathology v. Myriad Genetics*¹¹⁹ (henceforth the *Myriad (US)* case) where the Court held that isolated genetic material that is identical to the naturally occurring genetic sequence is unpatentable.^{120,121} The history leading to *Myriad (US)* is important for understanding the

¹¹⁴ For an in-depth account of this issue, see Dan L. Burk and Mark A. Lemley, 'Is Patent Law Technology Specific?' (2002) 17 Berkeley Tech. L.J. 1155; and Dan L. Burk and Mark A. Lemley, 'Policy Levers in Patent Law' (2003) 89 Virginia Law Review 1575.

¹¹⁵ Question of "patent-eligibility" concerns whether the subject matter of the application is a patentable invention under the relevant patent law. For example, in Europe, as part of the European Patent Convention, this requirement is regulated by Article 52 and Article 53 of the European Patent Convention, and in EU law by the Biotechnology Directive. In the U.S., as explained in the previous section, the common practice of the USPTO is that an invention is not patentable if it is a product of nature. Concerning biotechnological inventions, the U.S., the product of nature exception meant that the product was not patentable unless it was "isolated and purified from the surrounding environment". (See *Parke Davis & Co. v. H.K. Mulford Co.* 189 F. 95 (1911)) This principle encouraged patenting of isolated genetic sequences until the SCOTUS decision in the case of *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, where the Court held that isolated genes are not patentable. In Europe, both under the European Patent Convention and the Biotechnology Directive, genetic sequences are still patentable. (See Part C below.)

¹¹⁶ Question of "patent-worthiness" concerns whether the patent eligible invention meets certain substantive patentability requirements. In the U.S., these requirements are novelty, non-obviousness, utility, and sufficient disclosure. In Europe, under the European Patent Convention, these requirements are similarly novelty, inventive step, industrial applicability and sufficient disclosure.

¹¹⁷ Sherkow (n.111), p.164.

¹¹⁸ See example gene test in Part A above.

¹¹⁹ 133 S. Ct. 2107 (2013).

¹²⁰ *Ibid* at 2119.

¹²¹ The decision and reasoning of the SCOTUS will be discussed in the later in this section.

boundaries of both the legal debate and the public debate. Additionally, given the growth of personalised medicine applications, understanding this history may help guessing what may come next for the patentability of genetic inventions.

Timeline of the Scientific, Technological and Legal Developments¹²²

The scientific (and the resulting technological) developments in molecular biology changed the scope of patent applications. Patent applications evolved from claiming inventions concerning small molecular compounds to complex proteins to entire genes.

Correspondingly, the legal debate was shaped with the public reaction to patenting living material. Lets now move on to a summary of the central scientific and technological developments and the following legal developments in the U.S. eventually leading to the practise of the allowing patentability of isolated human DNA, and then recently overturning it.¹²³

(1) “The products of nature” doctrine: The patentable subject matter doctrine prohibits the inventions concerning “natural laws, phenomena, or products, or abstract ideas” to be patent eligible.¹²⁴ Early cases in the 19th century interpreting this doctrine did not grant patents to such inventions of the products of nature.¹²⁵

(2) *Race to isolate epinephrine (also known as adrenaline) between 1895-1904*: After the extracts of the adrenal gland were obtained in 1895, there was a race to isolate and purify the epinephrine (or adrenaline) hormone extracted from the adrenal gland. Finally in 1904, the hormone was first synthesized in a laboratory.¹²⁶

(3) Patentability of “isolated or purified” natural products in 1911: In 1901, the American pharmaceutical firm Parke-Davis & Co. obtained a patent on adrenaline. The validity of this patent was challenged in court on the ground that adrenaline was a

¹²² For more information see Sherkow (n.111).

¹²³ In the following timeline, the central scientific and technological developments are underlined and in italics, the legal and social developments are in bold.

¹²⁴ Sherkow (n.111), p.164; Rebecca Eisenberg, ‘The story of Diamond v Chakrabarty: Technological change and the subject matter boundaries of the patent system’ in Jane Ginsburg and Rochelle Cooper Dreyfuss (eds), *Intellectual Property Stories* (Foundation Press, 2005), p.334.

¹²⁵ For example, see the case of *Ex parte Latimer*, 1889 Dec. Comm’r Pat. 123.

¹²⁶ Kara Rogers, ‘Epinephrine’ in Encyclopaedia Britannica <<https://www.britannica.com/science/epinephrine#toc329394>> accessed on 26 September 2017.

product of nature. In the case of *Parke Davis & Co. v. H.K. Mulford Co* (1911).¹²⁷, Judge Learned Hand held the patent valid on the ground that the claimed adrenaline was ‘*isolated and purified from its natural surroundings*’ and thus it was ‘*not a product of nature*’. This principle later used in the patenting of early genetic material.

(4) The discovery of the structure of DNA double helix in 1953: James Watson and Francis Crick discovered the molecular structure of DNA in 1953.¹²⁸ Following this discovery, several patents were granted for nucleotide derivatives in the 1950s and 1960s.¹²⁹

(5) Increased patenting of products of biology in the 1960s: For example, one patent in 1969 claimed one strain of a rapidly reproducing RNA.¹³⁰ However, few of these patents were commercialised and enforced against infringers.¹³¹

(6) The discovery of reverse transcriptase in 1970:¹³² Reverse transcriptase is an enzyme that is used in genetic engineering for the formation of double-stranded DNA (cDNA) using the single stranded RNA (mRNA) as template.^{133,134}

(7) The development of the recombinant DNA technology in 1973:¹³⁵ In 1973, Stanley Cohen and Herbert Bayer developed recombinant DNA technology.¹³⁶ Recombinant DNA technology is used in genetic engineering in order to introduce genes from one source into another for creating genetically modified organisms.^{137,138}

¹²⁷ 189 F. 95 (1911).

¹²⁸ James D. Watson and Francis H. Crick, ‘A Structure for Deoxyribose Nucleic Acid’ (1953) 171 *Nature* 737.

¹²⁹ For example, in 1957, the researcher and Nobel laureate Har Gobind Khorana obtained a patent for ‘synthesized nucleoside polyphosphates’ in 1957 (U.S. Patent 2,795,580). Sherkow (n.111), p.164.

¹³⁰ D. Jachertz (1974) ‘Process for the enzymatic reproduction of informationally active RNA’ (U.S. Patent No: 3,785,926). Sherkow (n.111), p.165.

¹³¹ Ibid.

¹³² H.M. Temin and S. Mizutani, ‘RNA-dependent DNA polymerase in virions of Rous sarcoma virus’ (1970) 226 *Nature* (5252) 1211.

¹³³ ‘Reverse Transcriptase’ in Robert Hine and Elizabeth Martin (eds), *Oxford Dictionary of Biology* (7th edn OUP, 2016 Online Version)

¹³⁴ For more information see Part A(III) above.

¹³⁵ For a detailed discussion of this technology and patenting of recombinant products, see Sally Smith Huges ‘Making Dollars Out of DNA: The First Major Patent in Biotechnology and the Commercialization of Molecular Biology, 1974-1980’ (2001) 92(3) *Isis* 541.

¹³⁶ S.N. Cohen and others, ‘Construction of Biologically Functional Bacterial Plasmids in vitro’ (1973) 70(11) *Proc Natl Acad Sci U.S.A* 3240.

¹³⁷ ‘Recombinant DNA’ in Hine (n.133).

¹³⁸ Stazi (n.65), p.3.

(8) The first successful sequence of a full DNA molecule in 1977.¹³⁹

(9) Turning Points in 1980: Four consequent events marked the beginning of commercialisation of products of molecular biology:

a. *Diamond v. Chakrabarty*^{140,141} **(June 16, 1980):** The SCOTUS decision in *Diamond v Chakrabarty* marks the start of a new era in patent law concerning biotechnological inventions. In 1972, microbiologist Ananda Chakrabarty (working in the General Electric Company at the time) applied for a patent¹⁴² for oil-eating bacteria he created.¹⁴³ The patent claims included both the process of producing the bacteria and surprisingly also for *the bacterium itself*.¹⁴⁴ Although the claims for the process of constructing the bacteria were not problematic¹⁴⁵, the claims on the bacteria turned this application into a landmark case.

At first, the USPTO refused the patent on the ground that bacterium was a product of nature¹⁴⁶. The SCOTUS, on the contrary, held that this artificially created bacterium was a patentable invention with utility¹⁴⁷ because the oil-eating bacterium was a “manufacture” or a “composition of matter” within the meaning of §101¹⁴⁸. Rebecca Eisenberg explains this change of attitude as: “By the time the issue was presented to the Supreme Court, the anxiety surrounding genetic engineering in the 1970s had begun to subside, and medically important genes had been cloned in microorganisms. The commercial potential of biotech had become manifest, and a host of *amicus curiae* briefs from the scientific community urged the court to uphold the patentability of genetically engineered microorganisms.”¹⁴⁹ Moreover, quoting an earlier statement made in Congress, the SCOTUS held that “anything under the sun made

¹³⁹ F. Sanger and others, ‘Nucleotide sequence of bacteriophage phi X174 DNA’ (1977) 265 Nature (5596) 687.

¹⁴⁰ 447 U.S. 303.

¹⁴¹ For an excellent analysis of the case see: Matthew Rimmer, *Intellectual Property and Biotechnology: Biological Inventions*, (Edward Elgar, 2008), pp.24-49; Eisenberg, ‘The story of Diamond v Chakrabarty’ (n.124), pp.327–357.

¹⁴² Ananda Chakrabarty (1981) ‘Microorganisms having multiple compatible degradative energy-generating plasmids and preparation thereof’ (U.S. Patent No: 4,259,444).

¹⁴³ Eisenberg, ‘The story of Diamond v Chakrabarty’ (n.124), pp.332-333.

¹⁴⁴ Rimmer (n.141), p.27.

¹⁴⁵ The USPTO was already familiar with such claims and was granting patents to such claims. For example, Homme, Mancy and Ninet (1974) ‘Antibiotic 18.631 rp’ (U.S. Patent No: 3,793,147) for producing antibiotic 18.631 RP from microorganisms. Eisenberg, ‘The story of Diamond v Chakrabarty’ (n.124), p.333.

¹⁴⁶ Ibid.

¹⁴⁷ Rimmer (n.141), pp.25-26.

¹⁴⁸ Ibid, p.39.

¹⁴⁹ Rebecca Eisenberg, ‘Biotech patents: looking backward while looking forward’ (2006) 24(3) Nature Biotechnology 317.

by man”¹⁵⁰ was patentable subject matter.¹⁵¹ The main argument of the SCOTUS was twofold¹⁵²: (1) “Courts should not read into the patent law limitations and conditions, which the legislature has not expressed”¹⁵³; and (2) “rule that unanticipated inventions are without protection would conflict the core concept of the patent law that anticipation undermines patentability.”¹⁵⁴ In conclusion, setting the limits of patentable subject matter is the duty of Congress, and the Court believed Congress had already authorised patents for anything under the sun made by man.¹⁵⁵ Justice Burger, who delivered the majority opinion, also stated that the SCOTUS did not have the competence to examine the moral consequences of genetic engineering because that issue involved balancing competing values and interests. Hence, the issue was a matter for policy and needed to be resolved by the legislative.¹⁵⁶ This new doctrine paved the way for the later patent grants to animals, plants, and finally to *human genes*.

After the decision, although the SCOTUS urged Congress to take action concerning limits to patentable subject matter, Congress took no action.¹⁵⁷ Additionally, as it was evident that the SCOTUS was unwilling to affirm rejections to patentability of certain subject matter, this urged the USPTO to grant patents to similar inventions.¹⁵⁸ As the patents were not challenged on the grounds of invalidity, the only remaining way to challenge a grant was through infringement proceedings.¹⁵⁹ However, as the infringing defendants were commonly the competitors in the biotech industry, rather than challenging the patents on the patentable subject matter (because if they did so, their own patents would also be at risk), they challenged the patents on obviousness.¹⁶⁰ Lastly, after the decision, many companies started to apply for patents on their inventions that they were previously protecting via trade secrets.¹⁶¹ This shift

¹⁵⁰ Quoting H.R. Rep No. 1923 82d Cong. 2d Sess. (1952): “A patentable manufacture may include anything under the sun that is made by man.” So, if the government were to reverse its patent policy, it could address the issue again to legislate an exclusion. Eisenberg, ‘The story of Diamond v Chakrabarty’ (n.124), pp.350-51.

¹⁵¹ This is a very broad interpretation of the scope of patentable subject matter that is regulated under 35 U.S.C. §101.

¹⁵² Eisenberg, ‘The story of Diamond v Chakrabarty’ (n.124), p.352.

¹⁵³ 447 U.S. at 308.

¹⁵⁴ 447 U.S. at 316.

¹⁵⁵ Eisenberg, ‘The story of Diamond v Chakrabarty’ (n.124), p.352.

¹⁵⁶ Rimmer (n.141), p.38.

¹⁵⁷ Eisenberg, ‘The story of Diamond v Chakrabarty’ (n.124), pp.355-6.

¹⁵⁸ Ibid, pp.354-5.

¹⁵⁹ Ibid.

¹⁶⁰ Ibid.

¹⁶¹ Rimmer (n.141), p.43.

increased the dissemination of information and further contributed to the growth of the industry.¹⁶²

b. Genentech Inc.’s Public Offering (October 14, 1980): Genentech, a biotechnology company, filed for a patent application in 1979 concerning production of mammalian hormones including human insulin hormone.¹⁶³ When it offered one million shares valued at \$35 each in the following year, on the first day of trading, the value for one share reached \$88.¹⁶⁴ By the end of the day, the value of Genentech increased from \$36million to \$532 million.¹⁶⁵ This historic appreciation and profitability of Genentech was featured in Time Magazine in March 1981, with the headline “Shaping Life in the Lab: The Boom in Genetic Engineering”. This immediately caught the attention of the potential investors into the biotechnology industry.¹⁶⁶

c. First recombinant DNA patent (December 2, 1980): Stanley Cohen and Herbert Bayer were granted a patent for their invention of recombinant DNA technology.¹⁶⁷

d. Bayh-Dole Act (December 12, 1980): Before, any invention created with federal funding was at least partially owned by the federal government, and this discouraged universities and research institutions from investing into further research of applied sciences because they would not be able to commercialise their inventions.¹⁶⁸ With the Bayh-Dole Act, universities and research institutions could become patent owners of their own inventions, so they were encouraged for more research and development.¹⁶⁹

(10) “Anything under the sun made by man” doctrine: Following the decision in *Diamond v. Chakrabarty*, the “anything under the sun made by man” is patentable era had begun.

¹⁶² Ibid.

¹⁶³ Keiichi Itakura and Arthur Riggs (Genentech Inc.) (1987) ‘Recombinant cloning vehicle microbial polypeptide expression’ (U.S. Patent No: 4,704,362).

¹⁶⁴ Sherkow (n.111), 165.

¹⁶⁵ Rimmer (n.141), p.44.

¹⁶⁶ Ibid.

¹⁶⁷ Stanley N. Cohen and Herbert W. Boyer (1980) ‘Process for producing biologically functional molecular chimeras’ (U.S. Patent No 4,237,224).

¹⁶⁸ Sherkow (n.111), p.165.

¹⁶⁹ Ibid.

(11) The first gene patent granted in 1981¹⁷⁰

(12) *The race to map the human genome 1990-2003*: Until the announcement of the Human Genome Project (henceforth HGP), more than 1000 patents were granted to inventions claiming genes or genetic sequences, but only a few of them were patents claiming full-sequence human genes.¹⁷¹ The objective of the HGP was to sequence all of the nucleotides to determine the functions of all human genes.¹⁷² After the announcement of the publicly funded HGP, privately funded Celera Genomics joined the race to map the human genome. During the race, a debate began concerning the patentability of the short sequences of an expressed gene called “expressed sequence tags i.e. ESTs” used in sequencing. Although ESTs were held to be unpatentable on the ground of lacking utility in the case of *In re Fisher*¹⁷³, the issue of whether gene sequences were patentable or not still remained to be unresolved.¹⁷⁴ Consequently, after the completion of the HGP, thousands of patent applications claiming inventions concerning isolated human genes were filed.¹⁷⁵

(13) Increasing reactions to patenting of human biological material:

Following the case of *Moore v. Regents of the University of California*¹⁷⁶, when a patent was granted to an abnormal human cell line (Mo cells) from the spleen of a patient (John Moore) without the knowledge of the patient, the patient sued the patent holder for holding someone else’s property.¹⁷⁷ Although these claims were rejected by the Supreme Court of California, the case attracted intense public concern over the patenting of human body.¹⁷⁸

(14) Intense Public Debate on the Patentability of Genes in 2000s¹⁷⁹:

Although the USPTO has been patenting genes since 1980s, by early 2000s this practice has begun to be challenged by many public voices. In 2002, the UK-based Nuffield Council on Bioethics published a discussion paper titled “The Ethics of Patenting DNA”. In another paper by Jon Merz and Mildred Cho in 2005, aggressive patent strategies, of those companies

¹⁷⁰ Jack J. Manis (1981) ‘Plasmids and process of isolating same’ (U.S. Patent No: 4,273,875).

¹⁷¹ Sherkow (n.111), p.166.

¹⁷² Stazi (n.65), p.4.

¹⁷³ 421 F.3d 1365 (2005).

¹⁷⁴ See Rimmer (n.141), pp.138-163.

¹⁷⁵ Sherkow (n.111), p.167.

¹⁷⁶ 51 Cal. 3d 120 (1990).

¹⁷⁷ Hyo Y. Kang, ‘Processes of Individuation and Multiplicity: the Human Person in Patent Law relating to Human Genetic Material and Information’ (PhD thesis, European University Institute 2015).

¹⁷⁸ Sherkow (n.111), p.168.

¹⁷⁹ Ibid.

like Myriad, were heavily criticized for obstructing research and health care.¹⁸⁰ By 2006, the broader public started to be involved in the debate. In 2006, famous writer Michael Crichton published his new book *Next*, criticizing unwanted consequences of corporate greed in genetic research; and in 2007 penned an op-ed titled “Patenting Life” in the New York Times.^{181,182} In the U.S. Congress, a bill, HR 977, called “Genomic Research and Accessibility Act” prohibiting patenting of nucleotide sequences was introduced, but failed.

(15) The *Myriad* (US) Experience:¹⁸³ Myriad Genetics illustrates the evolution of the biotechnology industry. When Dr. Mark Skolnick and Nobel laureate Walter Gilbert founded Myriad Genetics in 1993, their business strategy was to focus on finding genes for diseases like cancer and developing genetic tests for individuals, rather than focusing on the development of new pharmaceuticals for treatment. This new business model meant growth in the market, because rather than targeting individuals looking for certain treatments, they now could offer their services to general public looking only for information on their likelihood of developing certain diseases.¹⁸⁴ In 1994, Myriad was able to isolate the location of the genes BRCA1¹⁸⁵ and BRCA2¹⁸⁶ and immediately upon discovery, it applied for product patents on the genes themselves. There are several statements by Myriad illustrating the vital role of acquiring such gene patents.¹⁸⁷

¹⁸⁰ Jon Merz and Mildred Cho, ‘What Are Gene Patents and Why Are People Worried about Them?’ (2005) 8(4) Community Genet., pp.203-208.

¹⁸¹ Michael Crichton, ‘Patenting Life’ *New York Times* (23 February 2007) <<http://www.nytimes.com/2007/02/13/opinion/13crichton.html?mcubz=1>> accessed 20 September 2017.

¹⁸² Sherkow (n.111), p.171.

¹⁸³ For an in-depth analysis see: Rimmer (n.141), pp.187-215; Davies, Kevin and Michael White, *Breakthrough: The Quest to Isolate the Gene for Hereditary Breast Cancer* (Macmillan Books, London 1995); C. Sevilla and others, ‘Impact of gene patents on the cost-effective delivery of care: the case of BRCA1 genetic testing’ (2003) 19(2) Int J Technol Assess Health Care, pp.287-300.

¹⁸⁴ Rimmer (n.141), p.187.

¹⁸⁵ In 1990, Mary-Claire King found that a gene located on Chromosome 17 (later to be named BRCA1) was responsible for breast cancer. J.M. Hall and others, ‘Linkage of early-onset familial breast cancer to chromosome 17q21’ (1990) 250 Science, pp.1684-9. The exact position of the gene was restricted down to about 1000 genes on chromosome 17. Finally, Myriad Genetics succeeded in sequencing the exact gene. Rimmer (n.141), pp.187-190.

¹⁸⁶ R. Wooster and others, ‘Localization of a breast cancer susceptibility gene, BRCA2, to chromosome 13q12-13’ (1994) 30 Science 265(5181), pp.2088-90.

¹⁸⁷ For example, Skolnick said “if it is not patented, you won’t get some group to spend money to develop it.” Rimmer (n.141), p.188. In 2001 Annual Report of Myriad, it is stated that: “Intellectual property is vital to Myriad. Accordingly, we have stepped up the pace of patent submissions to match the rapid discovery rate of potential therapeutic targets. To date, the company has submitted patent applications on over 1,800 genes, proteins, protein interactions, potential drug candidates, and predictive medicine opportunities.” Myriad Genetics, *2001 Annual Report* (Salt Lake City, 2001).

Following the publication of the scientific papers¹⁸⁸ on the discovery of BRCA1 and BRCA2 genes, Myriad filed patent applications concerning, among others, claims on the isolated sequences of BRCA1 and BRCA2 genes and their cDNAs. In accordance with the doctrines of patenting of products of nature if “isolated and purified from the surroundings” and “anything under the sun made by man is patentable”, the patents¹⁸⁹ were issued in 1998. Shortly after the grant, Myriad began to aggressively enforce its patents against clinicians and researchers. This stirred public concerns on the validity of patents held by Myriad on the grounds of their interference with scientific research, impact on patient access to treatment (because of the high costs of commercial genetic testing), and the administration of health care.¹⁹⁰ Sherkow and Greely point out that as a result of Myriad’s aggressive patent enforcement strategy, Myriad became “the scapegoat” for gene patenting.¹⁹¹ There were many other companies holding gene patents since 1980s, but none of the other gene patent holders enforced their patents as aggressively as Myriad.^{192,193} It was the aggression of Myriad and the fact that the patents under issue concerned one of the most common diseases worldwide that attracted wider public’s attention towards gene patenting and finally brought the problem of gene patenting to the courts.¹⁹⁴ The Federal District Court ruled against Myriad, and held the patents invalid.¹⁹⁵ The CAFC reversed this and ruled that the genes were patentable. When the case reached the SCOTUS, at first, in light of its recent decision in *Mayo v Prometheus*, the SCOTUS vacated the judgment of the CAFC and remanded the case back to the CAFC. However, the CAFC came to the same conclusion and when the plaintiffs again appealed the case to the SCOTUS, they were granted a writ of certiorari on the question of “*are human genes patentable?*”.

¹⁸⁸ Y. Miki and others, ‘A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1’ (1994) 266 *Science*, pp.66-71; S.V. Tavtigian and others, ‘The complete BRCA2 gene and mutations in chromosome 13q-linked kindreds’ (1996) 12 *Nature Genetics*, pp.333-37.

¹⁸⁹ For the BRCA1 gene, the patent granted was: Myriad Genetics, Inc. (1998) ‘17Q-linked breast and ovarian cancer susceptibility gene’ (U.S. Patent No: 5,747,282). For BRCA2 gene the patent granted was: Myriad Genetics, Inc. (1998) ‘Chromosome 13-linked breast cancer susceptibility gene’ (U.S. Patent No: 5,837,492).

¹⁹⁰ Rimmer (n.141), pp.188-189.

¹⁹¹ Sherkow (n.111), p.172.

¹⁹² *Ibid*.

¹⁹³ For example, the gene responsible for Huntington Disease was patented in 1987. (James F. Gusella (1987) ‘Test for Huntington’s disease’ (U.S. Patent No: 4,666,828)). However, there have been fewer complaints about the Huntington testing because the test was licensed at reasonable prices and the patent holder did not enforce his rights as aggressively. Jacob Sherkow and Henry Greely ‘The Future of Gene Patents and the Implications for Medicine’ (2013) 173(17) *JAMA Internal Medicine* 1569, p.1570.

¹⁹⁴ Sherkow (n.111), p.172.

¹⁹⁵ *Association for Molecular Pathology v. USPTO* 702 F.Supp.2d 181 (S.D.N.Y. 2010).

What had happened in Mayo Collaborative Services v. Prometheus Laboratories Inc.?

Prometheus's patent concerned the use of thiopurine compounds for treatment of certain autoimmune diseases such as Crohn's disease and ulcerative colitis. Although the utility of thiopurine for such diseases and the relationship between the toxicity and efficacy of thiopurine drugs and the metabolite levels in the bloodstream of the patient metabolizing the drug were known in the state of art at the time the patent application was made, the exact correlations between the metabolite levels and physiological effects were not known.¹⁹⁶

Prometheus' patent was based on its research findings regarding these correlations.

The claims in question claimed a process where a medical practitioner administers a thiopurine compound to a patient, and tests the level of resulting metabolite concentrations in the patient's blood. The metabolite levels are then checked against upper and lower metabolite limits that are disclosed in the patent, and the correlations that are observed are used to draw conclusions as to whether the patient is reacting positively or negatively to the drug, directing the practitioner to make suitable adjustments to the dosage.¹⁹⁷

The Court invalidated the claims, giving three main justifications for its decision: (1) The 'comparing' claims were protecting laws of nature; (2) the claims taken together did not add enough inventiveness to the law of nature to make the patent more than protection claimed simply over the law itself; and (3) the 'adjustment' claims merely involved "well-understood, routine, conventional activity, previously engaged in by researchers in the field".¹⁹⁸ The Court highlighted that granting patent protection on laws of nature risk "inhibit[ing] future innovation premised upon them, a danger that becomes acute when a patented process amounts to no more than an instruction to "apply the natural law"". ¹⁹⁹ According to Richard H. Stern who commented in detail on the case, four issues were resolved with the judgment in *Mayo Collaborative Services v. Prometheus Labs. Inc.*, namely, (1) patent-eligibility was re-emphasized as a preliminary inquiry in cases concerning claims applying laws of nature and abstract principles, (2) inhibition of future innovation remained an important policy goal in assessing patent eligibility, (3) mere implementations of natural laws and principles via obvious or conventional methods would likely be ineligible for patent protection, and (4) the Court as a methodology prefers to analytically dissect claims as opposed to considering them as a whole

¹⁹⁶ *Mayo Collaborative Services v. Prometheus Labs. Inc.* 132 S. Ct. 1289 (2012) at 1293 et seq.

¹⁹⁷ *Ibid.*

¹⁹⁸ Jacob S. Sherkow, 'And How: Mayo v. Prometheus and the Method of Invention' (2013), 122 Yale L.J. Online 315 p.351.

¹⁹⁹ 132 S. Ct. at 1301.

when considering patent eligibility.²⁰⁰ According to Sherkow and Greely, *Mayo Collaborative Services v. Prometheus Labs. Inc* will have a greater effect than *Myriad (US)* on decreasing incentives on patenting diagnostic uses of genes.²⁰¹

Myriad (US) SCOTUS Decision

Finally the SCOTUS held on June 13, 2013 that “a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but that cDNA is patent eligible because it is not naturally occurring”²⁰² because “separating a gene from its surrounding genetic material is not an act of invention.”²⁰³ This seems like a balanced decision. On the one hand, it calmed down the public concerns over gene patenting by invalidating patent claims on isolated sequences²⁰⁴, on the other hand, by leaving claims over cDNAs valid, it did not kill the sustainability of the biotech industry²⁰⁵. However, the decision is also criticized for creating more uncertainty in the patenting of genetic sequences.²⁰⁶ Rebecca Eisenberg notes that although the SCOTUS is the ultimate appellate jurisdiction in patent cases, “the Supreme Court’s sporadic interventions in the field have sometimes seemed like rules laid down by a noncustodial parent during weekend visits with the kids – at best, sparingly enforced once everyday life resumes under the supervision of someone whose judgment differs.”²⁰⁷

IV. Conclusion

Following the decisions in *Myriad (US)* (declaring claims on isolated gene sequences are invalid) and *Mayo v. Prometheus* (declaring ‘benchmarking’ method claims on genetic risk

²⁰⁰ Richard H. Stern, ‘Mayo v. Prometheus: no patents on conventional implementations of natural principles and fundamental truths’ (2012) 34 EIPR 502, pp.515-516.

²⁰¹ Sherkow (n.111), p.176.

²⁰² 133 S. Ct. at 2109.

²⁰³ Ibid at 2117.

²⁰⁴ For example, Harry Osterer, MD, who was among the plaintiffs, has stated, “the Court’s decision would help society feel more of the impact of genomics revolution.” G. Banks, ‘Justices reject patent on gene’ *Pittsburgh Post-Gazette*, (June 14, 2013), cited in Sherkow ‘The Future of Gene Patents’ (n.193), p.1569.

²⁰⁵ The Biotechnology Industry Organisation has noted that “the decision left intact patents on the synthetic transcripts i.e. cDNAs – commercially most important form of DNA used in biotechnology.” Biotechnology Industry Organisation, ‘Statement on US Supreme Court review of isolated DNA patents’ (BIO website, June 2013) <<https://www.bio.org/media/press-release/statement-us-supreme-court-review-isolated-dna-patents>> accessed 1 September 2017, cited in Sherkow ‘The Future of Gene Patents’ (n.193), p.1569.

²⁰⁶ Robert M. Schwartz and Timo Minssen, ‘Life after Myriad: the uncertain future of patenting biomedical innovation and personalised medicine in an international context’ (2015) 3 IPQ 189, pp.200-207.

²⁰⁷ Eisenberg, ‘The story of Diamond v Chakrabarty’ (n.124), p.330.

assessment are invalid), the future of gene patents remains to be uncertain.²⁰⁸ As Myriad Inc. was not enforcing its patents elsewhere as aggressively as it did in the U.S., it is unclear whether other jurisdictions will adopt the approach of the *Myriad (US)*.^{209,210}

Before we conclude this part, it is important to note that Myriad patents are still valid in Europe. They were challenged²¹¹ on the grounds for being against the *ordre public* and morality (under Article 53 of the European Patent Convention), not being novel, lacking inventive step and insufficiency of disclosure rather than being unpatentable subject matter because according to the Biotechnology Directive under EU Law, isolated sequences are expressly patentable.²¹² We now move on to an analysis of the European substantive law under the European Patent Convention and the Biotechnology Directive, in addressing the patentability of genetic sequences.

²⁰⁸ Sherkow (n.111), p.175; Christopher M. Holman, 'Mayo, Myriad, and the Future of Innovation in Molecular Diagnostics and Personalized Medicine,' (2014) 15 North Carolina Journal of Law & Technology 639.

²⁰⁹ For more information see Isabelle Huys and others, 'Gene and genetic diagnostic method patent claims: a comparison under current European and US patent law' (2011) 19 European Journal of Human Genetics, pp.1104-1107; Naomi Hawkins, 'A red herring: invalidity of human gene sequence patents' (2016) 38 EIPR 83; Geertrui Van Overwalle, 'Policy Levers Tailoring Patent Law to Biotechnology: Comparing U.S. and European Approaches' (2011) 1 UC Irvine L. Rev. 433; Luigi Palombi, 'Association for Molecular Pathology v Myriad Genetics (US) and D'Arcy v Myriad Genetics (AU): are gene patents in Europe a threatened species?' (2016) 38 EIPR 231; Ann Kurts, 'Consequences of the US Supreme Court decision on gene patenting' (2013) 53 EIPR 629.

²¹⁰ Following *Myriad(US)* the Australian High Court also invalidated Myriad's patent claims on BRCA1 and BRCA2 genes. *D'Arcy v Myriad Genetics Inc* [2015] HCA 35 (HC (Aus)).

²¹¹ *Breast and ovarian cancer/University of Utah* (T1213/05) of 27.9.2007 (Technical Board of Appeal); *BRCA2/University of Utah* (T0156/08) of 14.1.2011 (Technical Board of Appeal); *BRCA2/Cancer Research Technology* (T0902/07) of 7.9.2010 (Technical Board of Appeal); *Mutation/University of Utah* (T0666/05) of 13.11.2008 (Technical Board of Appeal).

²¹² See Gert Matthijs and others 'The European *BRCA* patent oppositions and appeals: coloring inside the lines' (2013) 31(8) Nature Biotechnology, pp.704-710.

C. EUROPEAN PATENT SYSTEM'S RESPONSE TO GENE PATENTS

I. Introduction: General Starting Points

The complexity of the European patent system is such that some authors to call it byzantine²¹³. Unlike in the U.S., what is called the European patent system does not rest on a singular centralised system. Its complexity stems from the presence of multiple ways for securing a patent, multiple sources of law and international treaties urging for harmonisation at the European and international level, multiple interpretations of the two main texts²¹⁴ regulating the substantive European patent system, and lack of a central authority²¹⁵ setting precedents and providing legal clarity and certainty. This complex structure will not be explained nor analysed in detail in the following pages, as this is a separate and complex topic in itself that remains outside the aim of this section. However, it is important to note that European Union (henceforth EU) lawmakers' intention to establish a Unified Patent Court is, *inter alia*, motivated by the need to alleviate this byzantine complexity.

For the purposes of this paper, the responses to gene patents of the two legal texts providing for and regulating the substantive patent law at the European level will be analysed in detail. The first text is the European Patent Convention of 1973 (henceforth EPC), an international agreement between its contracting states in Europe, which include all the EU Member States, though EU is not a party this international treaty. The second text, Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions²¹⁶ (henceforth the Biotech Directive), is specifically designed by EU lawmakers to address the problems emerged in the interpretations of the EPC system vis-à-vis the biotechnological inventions. So, for the purposes of the following sections, what is meant by the European patent system is the patent law under the EPC and the Biotech Directive.

²¹³ W. Cornish and others, *Intellectual Property: Patents, Copyright, Trade Marks and Allied Rights*, (8th edn Sweet & Maxwell, London 2013), p.121.

²¹⁴ Namely the European Patent Convention 1973 (henceforth EPC) and Directive 98/44/EC (henceforth the Biotech Directive)

²¹⁵ Foundational work for the Unified Patent Court is under way, however, for the purposes of this paper the development of the UPC is left outside the scope of the discussed issues.

²¹⁶ Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, [1998] OJ L 213/13.

The U.S. patent system and the European patent system have roots in similar justifications for patent grants and similar provisions in substantive patent law standards, so it can be expected that they would eventually operate in a similar manner. Regardless, the European authorities since the creation of the EPC in 1973 have aimed to harmonise the European patent system with the U.S. patent system as much as possible, not merely by according the core patentability principles with those of the U.S. patent system, but creating a competitive yet similar system for international trade relations. In the previous section, the U.S. approach to gene patentability has been explored in order to better comprehend the European patent system as the U.S. patent system have provided guidance for the younger European patent system.²¹⁷ However, there are still important differences existing between the U.S. system and the European system that are important to make a note of. Such differences include but are not limited to²¹⁸:

- (1) Intellectual property right is a constitutional right in the U.S., which means the U.S. Constitution creates the right, whereas it is a national right in Europe, meaning there is no centralised legislation or a competent central court enforcing the right.²¹⁹
- (2) In the U.S., the USPTO, a centralised institution of the federal government, grants patents, whereas, for the European states under the EPC, the European Patent Office (henceforth EPO) grants the patents and the EPO is not a EU institution.^{220,221}
- (3) Patents are important for the U.S. national policy “to promote the progress of science and useful arts”²²² so to create new industries, whereas the policy motivation of the European Commission for a European patent system is to avoid barriers to trade that would impede the proper functioning of the internal market.^{223,224} The Preamble of the EPC states “strengthen(ing) co-operation between the States of Europe in respect of the protection of inventions” as one of its policy motivations.²²⁵

²¹⁷ To repeat, my reference to the European patent system should not be taken as a reference to the individual patent systems of European states, some of which have patent law histories that predate the U.S. by centuries.

²¹⁸ Oliver Mills, *Biotechnological Inventions. Moral Restraints and Patent Law* (Ashgate, 2005), pp.5-7.

²¹⁹ *Ibid*, p.5.

²²⁰ Obtaining a patent through the EPO procedure is not the only way to secure a national patent in the signatory states. The other ways are through the national patent offices or the hybrid system of the Patent Cooperation Treaty. The ‘European patent with unitary effect’ under EU law is at its final stage of adoption, and is expected to enter into force soon.

²²¹ Mills (n.218), p.5.

²²² U.S. Constitution, Article I, Section 8, Clause 8.

²²³ Biotech Directive, Recital 5.

²²⁴ Mills (n.218), p.6.

²²⁵ EPC, Preamble.

- (4) The U.S. system is older, thus the U.S. patent system has been tested more than the European patent system.²²⁶
- (5) The U.S. courts have developed the conditions for patentability whereas in Europe the EPC and the Biotech Directive provides the conditions for patentability. For example, in the U.S., the Courts have decided what patentable subject matter are, whereas in Europe, only the EPC provides guidance on what patentable subject matter *may not be* – the related provision of Article 52 has been drafted in defining what may be patentable in a negative manner creating complexities and uncertainties in determining what *may be* patentable. Thus, what is patentable in the U.S. law is clearer, which might cause patent applicants to feel more secure in the U.S..²²⁷
- (6) And finally, the European patent system has been referred to as “ask moral questions first, then patent”, whereas the U.S. patent system has been defined as “patent first, ask moral questions later.”²²⁸

These points provide a brief outline of the European patent system vis-à-vis the US patent system and make note of the important problematic aspects of the European system.

Let’s move on to the patentability criteria in the European patent system. The criteria can be described in a three-tiered test. The first tier preoccupies itself with the patentable subject matter, corresponding to the question of “is it patent eligible?” as asked previously in the U.S. patent system section. Here, the claimed invention in the application is evaluated under the negative description of patentable subject matter of Article 52 of the EPC, and *inter alia*, the morality exclusion from patentability under Article 53 of the EPC. If the application passes this tier, it moves to the second tier and the invention’s novelty, inventiveness and industrial applicability are examined. This second tier corresponds to the question of “is it patent worthy?” in the U.S. patent system. Finally, in the last tier, as per the disclosure requirement – which constitutes the main social justification for the state to granting this time-limited monopoly – (i) the sufficiency of the claims enabling the performance of the invention and relatedly (ii) the breadth of the claims important in determining the scope of the monopoly, are assessed. This three-tiered patentability test is the backbone of the European patent

²²⁶ Mills (n.218), p.6.

²²⁷ Ibid, p.7.

²²⁸ Stazi (n.65), p.185.

system as it is set by the EPC and transposed into the national patent laws of its contracting parties.

This three-tiered system poses difficulties when it is dealing specifically with gene patents. Although gene patents have been discussed vis-à-vis patentable subject matter (the debate on discovery vs. invention) and the morality of patenting genetic sequences, Cornish and others summarise a number of other concerns eventually resulting in including but not limited to the over-patenting of genetic sequences²²⁹:

- (1) Novelty and inventiveness requirements are interpreted very widely and a low threshold in both tests has been applied to patent applications concerning genetic material. This has been very much in the applicant's or patentee's favour. For early stages of complex new technology, it is understandable that any patent application is to be conceived as dramatically original and inventive to the eye of the patent examiner, and it is only when the examiners become increasingly familiar with the technology, they can start assessing the invention's true novelty and inventiveness.²³⁰
- (2) A patent may have been granted before the invention has demonstrated its industrial applicability, so the scope of the monopoly granted may have been unfairly wide and disproportional to the invention disclosed.²³¹
- (3) Concerns numbered (1) and (2) result in over-patenting of genetic sequences. Over-patenting will result in a crowd of too many closely related patents to different parties, and this may create a 'tragedy of the anti-commons' in the space needed to keep conducting research and development in genetic technologies and genomic sciences, and moreover, the exceptions for experimental use are too narrow.²³²

²²⁹ Cornish (n.213), p.907.

²³⁰ Ibid, p.908.

²³¹ Ibid, p.909.

²³² Other than a brief introduction to experimental use in Part D, this issue is not within the scope of this paper but for further information see: ibid, pp.911-914; Geertrui van Overwalle (ed), *Gene Patents and Collaborative Licensing Models: Patent Pools, Clearing Houses, Open Source Models and Liability Regimes* (CUP, 2009); Garrett Hardin, 'The Tragedy of the Commons' (1968) 162 Science 1243; Michael A. Heller, 'The Tragedy of the Anticommons: Property in the Transition from Marx to Markets' (1998) 111(3) Harvard Law Review 621; Michael A. Heller and Rebecca S. Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research' (1998) 280 Science 698; Geertrui Van Overwalle, 'Exclusive ownership versus open commons: the case of gene patents' (2013) 4 WIPO J 139.

- (4) As a result of these practices, the application of current patent law to the genetic sequences creates too many gene patents held by too few companies and consequently too few genetic diagnostics tests are available for the public.²³³

There are proposed solutions dealing with these noted concerns, namely an over-arching and broadened industrial applicability test proposed by the Biotech Directive, widening the scope of experimental use and compulsory licensing²³⁴, and the possibility of non-patent law solutions for genetic inventions such as through protection of genetic databases, a new *sui generis* gene right and protecting genetic inventions via trade secrets.²³⁵ Because each one of these could be developed into papers on their own, the main focus of this part will be on the over-arching industrial applicability criterion under the Biotech Directive. This paper will only briefly introduce a *sui generis* gene right proposed in the literature in Part D.

To begin, it is deemed essential to understand the roots and justifications of the European patent system, because the essential concepts are the engines that drive the whole system, but because they lack clear definitions, they can only be understood by looking at the evolution of the system. Therefore, in the following sections, a brief history of the European patent system will be explored and a brief discussion of the justifications for granting patents will be presented.

II. A Brief Historical Account of the Development of the European Patent System

The idea of granting a monopoly in order to incentivise innovation has old roots.²³⁶ Its origins could be traced back to the enactment of the Statute of Monopolies 1624 in England as providing the statutory basis for the development of modern national patent systems that are currently in force.²³⁷ According to Machlup and Penrose “apart from its expression in statute

²³³ Cornish (n.213), pp.915-917.

²³⁴ See Pozo (n.106), Chapter 7.

²³⁵ Esther Van Zimmeren and Geertrui Van Overwalle, ‘A paper tiger? Compulsory license regimes for public health in Europe’ (2011) 42 IIC 4; Robert Cook-Deegan and others, ‘The next controversy in genetic testing: clinical data as trade secrets?’ (2013) 21 European Journal of Human Genetics 585.

²³⁶ Cornish (n.213), p.122.

²³⁷ F. Machlup and E. Penrose, ‘The Patent Controversy in the Nineteenth Century’ (1950) 10 Journal of Economic History 1, p.2.

form, the patent system is not predominantly an English creation.”²³⁸ Also, according to them, “if the Statute of Monopolies has been called the Magna Carta of the rights of inventors, it is not because it originated patent protection for inventors but chiefly because it laid down the principle that only a ‘true and first inventor’ should be granted a monopoly patent.”²³⁹ By the end of the 18th century, two other major trading countries had statutory patent systems: The French Constitutional Assembly passed a patent law in 1791 and the Congress in the United States passed the first patent law in 1793.²⁴⁰ During the next half-century, the concept of a patent system spread to other countries – e.g. Austria in 1810, Prussia in 1815, Belgium and the Netherlands in 1817, Sweden in 1834, Portugal in 1837 *etc.* Since then, the legal landscape of the patent system both at the international level, and more important for the purposes of this section, at the European level, has changed drastically.

i) The Statute of Monopolies 1624 of England

Since the fourteenth century, the Crown of England granted royal privileges to foreign craftsmen by way of letters patent.²⁴¹ The prime motivation for this practice was to encourage foreign craftsmen to live and to practice their trade in England, so eventually the local population would acquire the foreigners’ skill, as a consequence the introduction of new industries was expected to help England’s economy to strengthen in the long run.²⁴² However, unlike the current patentability requirements of the modern patent system, there were no set of requirements for examining patent eligibility or patent-worthiness of the craft before issuing the letters patent. The result was the presence of arbitrary large monopolies

²³⁸ Ibid. It is widely accepted that the Statute of Monopolies 1624 of England established the first patent law of in the modern sense, and it evolved from the system of royal privileges. This statement is somewhat correct. However, both in Europe and other places in the world such as China, around the same time period, similar systems for granting privileges for inventions could be found. In various European countries in the 16th and 17th century the practice of granting monopoly privileges to innovators existed. For example, the Venetian Patent Statute of 1474 established the first statutory patent system in Europe and is deemed as the earliest codified patent system in the world. It provided ten-year exclusive privileges to “any new and ingenious device, not previously made, provided it was useful.” Although these principles remain relevant in the current patent law, since Venetian law did not go beyond codifying prior customs and did not establish any new principles, the Venetian law is not usually cited in the literature as the beginning of the modern patent system. Tanya Aplin and Jennifer Davis, *Intellectual Property Law: Text, Cases and Materials* (2nd edn OUP, 2013), p.535.

²³⁹ Machlup (n.237), p.2.

²⁴⁰ Before the enactment of the first federal patent statute of the U.S. (the Patent Act of 1790 which was later replaced by the Patent Act of 1793) the U.S. Constitution adopted on September 17, 1787 had (and still has) a provision for protecting intellectual property. Article I, Section 8 states: “The Congress shall have power to promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries.”

²⁴¹ Letters Patent was a legal instrument in the form of a public written order (or any type of document) issued by a monarch generally granting a right, monopoly, title, liberty, honours or status.

²⁴² Tanya Aplin and Jennifer Davis, *Intellectual Property Law: Text, Cases and Materials* (2nd edn OUP, 2013), p.535.

that artificially raised prices.²⁴³ Consequently, the English Parliament introduced a general prohibition on the grant of patents with the Statute of Monopolies in 1624 except for what is provided for under section 6:²⁴⁴

“Provided that any declaration before shall not extend to any letters patent and grants of privilege for the term fourteen years²⁴⁵ or under, hereafter to be made, of the sole working or making of [1] *any manner of new manufactures* within this Realme, to [2] *the true and first inventor* and inventions of such manufactures which others at the time of making such letters and grants shall not use, so as [3] *also they be not contrary to the law, or mischievous to the State, by raising prices of commodities at home, or hurt of trade, or generally inconvenient*; the said fourteen years to be accounted from the date of the first letters patents or grant of such privilege hereafter to be made, but that the same shall be of such force as they should be if this act had ever been made, and of none other.”²⁴⁶ *[emphasis added]*

Section 6 is often regarded as “an act of economic policy” rather than “providing justice and reward for the intellectual efforts of the inventor”²⁴⁷ and as laying the foundational principles of patent law, which are: [1] delimiting what is patentable to “any manner of new manufactures”; [2] confiding the patent holder to be only “the true and first inventor” –the inventor was understood to be not only the one who devised the manufacture but also the one who imported it²⁴⁸; and [3] restricting the system to the boundaries of favouring public interest. To draw parallels with the current legal framework, the first of these three principles can be understood as an early positive description of today’s “invention” requirement; the second principle as developed into “the novelty test” with time, and the third principle as evolved into “the morality exception”. However, it might be misleading to trace patent law back to 1624 Statute of Monopolies because this creates the illusion that patent law is essentially timeless, unconditional and undisputed, and eventually deter any discussion for the legitimacy and functioning of the system.²⁴⁹ It is important to note that neither intellectual

²⁴³ A famous example being the grant of a monopoly over playing cards: *Darcy v Allen* (1602) 77 ER 1260.

²⁴⁴ Aplin (n.242), p.535.

²⁴⁵ This period was based on the idea that the patentee would teach the new craft to two of his apprentices.

²⁴⁶ The Statute of Monopolies 1623 (of England), section 6.

²⁴⁷ Cornish (n.213), p.123.

²⁴⁸ Ibid, p.122.

²⁴⁹ Brad Sherman and Lionel Bently, *The Making of Modern Intellectual Property Law* (CUP, 1999), pp.208-9.

property law as known today nor patent law existed before the mid-19th century.²⁵⁰ There were forms of intellectual property as seen under Section 6, but they were far from organised, distinguished and clear legal instruments.²⁵¹

ii) The Patent Controversy of the Nineteenth Century²⁵²

The 17th century “provided no more than a germ of a functioning patent system.”^{253,254} For example, the requirement of providing a written description of the invention did not emerge until the 18th century and disclosing a written specification became *quid pro quo* for the patent granted.²⁵⁵ However, the early practice of disclosure of the invention was inefficient, insufficient, and often disproportionate to the protection granted.²⁵⁶ In the 19th century, the discontent with the patent system led to intense disputes on the validity of the patent system.²⁵⁷ The subject of patent reform first caught attention of the legislature in England, and then the subject ignited a larger debate on the existence and justification of patent systems across Europe.

Generally, the main argument of patent abolitionists stemmed from free-trade arguments. In Germany, economists were almost unanimous in the disapproval of the system, in Switzerland, political economists declared that the principle of patent protection was ‘pernicious and indefensible’, and in Holland, the anti-patent movement, even more than

²⁵⁰ Ibid, pp.93-110.

²⁵¹ Ibid, pp.2-3.

²⁵² See Machlup (n.237); Cornish and others, *Oxford History of the Laws of England* (Vol. XIII OUP, 2010) for more in depth account of the debates.

²⁵³ Cornish (n.213), pp.123.

²⁵⁴ However, it is important to note that the essential *quid pro quo* of granting patents then putting the invention into practice (so that a new industry would be introduced), rather than the sufficient disclosure of the knowledge of the invention, which is the current predominant *quid pro quo* for granting patents. D. Seaborne Davies, ‘The Early History of the Patent Specification’ (1934) LQR 86; and E. Wyndham Hulme, ‘On the Consideration of the Patent Grant, Past and Present’ (1897) LQR 313 cited in Aplin (n.242), p.536.

²⁵⁵ For example, see Lord Mansfield judgment in the English case of *Liardet v Johnson* (1778) 62 ER 1000 cited in ibid. According to E. Wyndham Hulme, this shifting of the consideration of the patent grant from practising the invention to disclosure of the invention led to a corresponding change in the conception of novelty. In assessing novelty it is now pertinent to ask if the trade already knew of the invention through publication. E. Wyndham Hulme, ‘On the History of Patent Law in the Seventeenth and Eighteenth Centuries’ (1902) 18 LQR 280 cited in Aplin (n.242), p.536.

²⁵⁶ Cornish (n.213), p.123.

²⁵⁷ The three main complaints were: (1) the administration for securing a patent was too cumbersome; (2) the cost of obtaining a patent was too high; (3) the ground to declare a patent invalid was too rigid. Aplin (n.242), p.536; H. I. Dutton, *The Patent System and Inventive Activity during the Industrial Revolution, 1750-1852* (Manchester University Press, 1984), pp.34-36.

elsewhere, was linked with the free-trade movement.²⁵⁸ However, the controversy concerning patent law was not a debate on free-trade movement versus protectionism; the main concerns were about the efficient functioning of the patent laws and the difficulties of reform. In order to disengage the patent system from monopoly and free trade issues, the patent advocates provided justifications for the system that relied on natural law, social justice and utilitarian theories. Eventually, the patent advocates won the debate and the victory was later evidenced by the subsequent actions of legislations enacting national patent statutes in the various countries. According to Machlup and Penrose, the best explanation of the sudden disappearance of the anti-patent movement is the simultaneous weakening of the free-trade movement in Europe in consequence of the severe depression in the second half of the 19th century.²⁵⁹ The debate has long subsided, but the justifications employed by the patent advocates still have relevance because their arguments helped shape the legal foundations of modern patent law.²⁶⁰

iii) Post-World War II

The 20th century saw two main developments in the patent system. First, the European Economic Community was founded, and immediately after the creation of a single patent granting office, the EPO, and harmonisation of national patent standards, through the EPC, followed. As patents of different standards would impede intra-community trade, with the creation of the EPC and the EPO European nations aimed to overcome patent-related barriers to European trade. Additionally, foundations of a single community patent that would be effective throughout the then European Economic Community, an idea applied today in the EU as the *European patent with unitary effect* or simply the Unitary Patent, was started to be built shortly after.

Secondly, the general approach to patentability shifted from restricting patents to favouring patents. Although many reforms took place to accommodate many criticisms of the 19th century debates such as the detrimental effects of granting a monopoly right²⁶¹, the need for an accessible and efficient administration of granting a patent²⁶², and avoiding granting

²⁵⁸ Machlup (n.237), p.5.

²⁵⁹ Ibid, p.6.

²⁶⁰ Sherman (n.249), pp.152-7.

²⁶¹ Aplin (n.242), p.538.

²⁶² Ibid.

patents for unmeritorious inventions²⁶³, the effects of the criticisms were still evident in the reluctant attitude of the courts in granting patents for being contrary to public interest.²⁶⁴ However, after the Second World War this reluctant attitude changed both in national courts and in the EPO. For example in the English case of *Ethyl Corporation's Patent*²⁶⁵ the court stated that: "The climate of opinion has changed. It is now generally recognized that it is in the public interest to encourage inventive genius. Accordingly the modern tendency of the courts has been to regard patent claims with considerable favour than before."²⁶⁶

This change in attitude is reflected as opting for a broader interpretation of the patentability principles. It also coincides with the post-war economic depression, the following industrial boom in Europe, and the development of pharmaceutical technologies. However, the broad interpretation of the concept of patentable invention came at the expense of non-patentable discovery.²⁶⁷ With the development of pharmaceutical technologies, patent applications for chemical inventions concerning novel molecules soared both in the U.S. and Europe. For some time, any novel molecule whose 'industrial applicability' concerned further research purposes would be patentable and this fact also satisfied the 'inventive step' requirement.²⁶⁸ With the advent of biotechnology, the practice of patenting early genetic material followed. Genetic material has been deemed patentable by way of applying the same approaches and the same broad interpretation to the patentability principles undertaken for the earlier patenting of chemical inventions concerning novel molecules. Eventually, courts both in Europe and the U.S. limited such broad practices in fairly recent decisions.

This is as brief as one can get when explaining the history and evolution of the patent system. There are many detailed accounts of the history of patent law, but for the purposes of this paper and for the later sections, the stated turning points of this long history is sufficient.²⁶⁹ These turning points in history are important in understanding the current legal framework with respect to patents concerning genetic inventions. It might also be thought that the past is irrelevant and obsolete ever since intellectual property law and more specifically patent law has started to interact with the new types of organic and genetic property. The challenge

²⁶³ Ibid.

²⁶⁴ Lionel Bently and Brad Sherman, *Intellectual Property Law* (4th edn OUP, 2014), p.378.

²⁶⁵ [1972] RPC 169.

²⁶⁶ Ibid at 193.

²⁶⁷ Bently (n.264), p.898.

²⁶⁸ Ibid.

²⁶⁹ For an excellent account of the modern intellectual property law see Sherman (n.249).

posed by the advent of genomic technology complicated the relationship between the law and intangibles, generally speaking. However, rather than creating a ‘new order’ of intellectual property law, it might be useful to consider the evolution of the concepts in trying to formulate a doctrine of intellectual property that can accommodate any new type of intangibles created by advancing technologies.²⁷⁰

Now, we shall briefly examine justifications for patent protection. This will be helpful when we move on to analyse the evolution of patentability requirements vis-à-vis genetic inventions under the EPC and EU law.

III. Justifications for a Patent

i) The nature of Intellectual Property

Before moving to the specific justifications for a patent, let's briefly return to the basics of the intellectual property law and the nature of a patent in order to build up on the fundamental justifications for a patent grant. The following account is important to comprehend the justifications for patent law. Generally speaking, intellectual property law claims to protect “the finer manifestations of human achievement” and the ultimate policy shaping the governing rules of intellectual property law is securing the outcomes of exclusive rights created by intellectual property in order to uphold the *quid pro quo* rationale of granting patent protection.²⁷¹ Essentially, intellectual property law aims to protect applications of ideas and information –in other words “the products of the human intellect”²⁷², that are of commercial value.²⁷³ Furthermore, it is growing more in importance as the development of new technologies that depend on the exploitation of ideas and knowledge become increasingly crucial in securing growth in national economies and in creating leverage over other countries in global trade.²⁷⁴ Although the subject matter of different intellectual property rights cover the various fields of “manifestations of human achievement”, one characteristic that is shared by different types of intellectual property rights is that they are all negative rights i.e. they all

²⁷⁰ Ibid, pp.1-7.

²⁷¹ Cornish (n.213), p.4.

²⁷² Bently (n.264), p.1.

²⁷³ Cornish (n.213), p.6.

²⁷⁴ Ibid.

forbid third parties from doing certain things with the subject matter of the right.²⁷⁵

Intellectual property gives the right holder exclusive control over the activities of others and the right to commercially exploit the related protected subject matter.

ii) Nature of Patents

According to Bently and Sherman a patent is understood today as “a limited *monopoly* granted in return for the *disclosure* of technical information”²⁷⁶ [*emphasis added*]. Of all the different types of intellectual property rights, the patent is the only intellectual property granting a true monopoly and the ability to charge a monopoly price to the patentee, for creating an *invention* regardless of whether the invention provides great contributions to the accumulation of human knowledge or just small contributions or even trivial improvements to the existing knowledge or to the inventions of others, as long as it has *industrial value*. Essentially, for the said reasons of the nature of a patent, a patent is potentially the most economically valuable yet also the most dangerous of all the intellectual property rights.²⁷⁷ At the core of patent law lies the concept of absolute exclusivity: (1) Patents confer the patentee an exclusive right to prevent imitators from exploiting the same invention; but at the same (2) it confers the exclusive right to also exclude any third party, who has independently developed the same invention too, from making and selling the invention.²⁷⁸

Therefore, leaving aside the specific legal tests encoded in the legal systems for granting a patent, the most basic patent principles can be summarised as follows:

A patent grants the patentee;

- a limited *monopoly*;
- for an *invention*; [Recall: Under the Statute of Monopolies 1624, an invention is formulated positively as a manner of new manufacture]
- that has *industrial value*; [Recall: In the early patent law has been developed for the introduction of new crafts, i.e. new industries, into the local economy]

²⁷⁵ Ibid.

²⁷⁶ Bently (n.264), p.376.

²⁷⁷ Cornish (n.213), p.8.

²⁷⁸ Aplin (n.242), p.539.

- for exchange of *disclosure*. [Recall: The disclosure requirement was introduced later as a consideration on part of the patentee as an effort to cope with the effects of industrialisation and increasing demand for patents and patent applications.]

iii) Justifications for Patents²⁷⁹

Despite the many conflicting theories about why people abide the law, it is common sense that for lawmaker and adjudicator, it is important to be aware of the values generally upheld in a society when distributing rights and balancing competing interests of the parties involved in a legal dispute. This is why theoretical accounts of intellectual property are important. They employ a normative role in assessing the substantive rules at play and offer a way to reflect and criticize these substantive rules.²⁸⁰ When European courts, institutions, and administrative bodies engage in teleological, systemic and purposive interpretation of the substantive law(s), the issue of whether their assessment coincides with the common values of the European societies is commonly raised.²⁸¹ For this reason, we will now very briefly touch upon the main theories that justify intellectual property. We will then look closely at whether or not the current biotechnological patenting legal framework employs any of these values and justifications in the following section. It is important to note that although each theory has a good share of criticism, this will not be addressed for the purposes of this paper.

a. Natural Law Theories

Natural law theories can stem from two different premises:

- (1) Creation of any type of tangible and intangible property including intellectual property is an extension of the personality of the creator; thus, it is a manifestation of the creator's personhood.²⁸² As Hegel states: "A person must give to his freedom an external sphere, in order that he may reach the completeness implied in the idea."²⁸³

²⁷⁹ For an in-depth discussion see: Justine Pila and Paul L. C. Torremans, *European Intellectual Property Law* (OUP, 2016), pp.74-108; Peter Drahos, *A Philosophy of Intellectual Property* (Dartmouth Publishing Company, 1996); Robert P. Merges, *Justifying Intellectual Property* (Harvard University Press, 2011); Cornish (n.213), pp.143-154; Machlup (n.237).

²⁸⁰ Pila (n.279), p.74.

²⁸¹ Ibid, p.75.

²⁸² Ibid, pp.86-88.

²⁸³ S.W. Dyde (tr), G.W.F. Hegel, *Philosophy of Right* (Batoche Books, 2001), p.55.

- (2) A person has natural property in her own ideas because of the labour involved in the creation of the intellectual product. As Locke states: “Whatsoever then he removes out of the state that nature hath provided, and left it in, he hath mixed his labour with, and joined it to something that is his own, and thereby he makes it his property.”²⁸⁴ Therefore, as the creator mixes her labour, and she invests his time, money, energy in developing an intellectual product, natural theorists argue that the creator should be rewarded with proprietary rights to the product.

b. Justice or Fairness Theories

According to these theories, justice requires that a person receives reward for his services in proportion to his invention’s usefulness to the society and it is the moral duty of the society to secure a just reward for the useful services of the inventor and to prevent free riders to benefit from another’s labour and become unjustly enriched. The most appropriate way to secure a just reward to inventors is by means of exclusive patent rights in their inventions.²⁸⁵

c. Instrumentalist Theories²⁸⁶

Utilitarian explanations for intellectual property aim to reach maximization of intended social benefits and eventually provide more benefits than harms to the society²⁸⁷ for ultimately encouraging certain types of social behaviour and discouraging undesirable social behaviour.

Two main incentives can be discussed:

- (1) “The Best Incentive to Invent Argument”²⁸⁸: A society needs industrial progress for economic prosperity, and inventions are necessary to secure such progress. However, inventors won’t invent unless they have hopes that they can profit from their inventions. The simplest, the cheapest, and the most effective way for society to secure such a desirable behaviour of investing in inventions, is by granting exclusive patent rights to inventors.

²⁸⁴ John Locke, *Second Treatise of Government* (Hackett, 1980), p.19.

²⁸⁵ Pila (n.279), pp.90-93; Machlup (n.237), pp.17-21.

²⁸⁶ Drahos (n.279), pp.199-224.

²⁸⁷ Pila (n.279), pp.93-94.

²⁸⁸ Machlup (n.237), p.10.

- (2) “The Best Incentive to Disclose Secrets Argument”²⁸⁹: A society needs industrial progress for economic prosperity, and inventions are necessary to secure such progress. It is necessary for new inventions to be known by the general public for other inventors to build upon the existing technology. However, if the society grants no protection against imitation, the inventor will keep his invention as a secret. This is socially undesirable behaviour because when the secret dies with the inventor, the society will lose the new art. The best way to discourage this behaviour is by granting exclusive patent rights in exchange for public disclosure of the secret.

iv) Gene Patenting in the light of Justifications for Patents

The main discussion for patents revolves around the utilitarian perspective on intellectual property against a rights-based natural rights perspective on intellectual property. This discussion can be formulised as: “*Should the inventors have inherent rights in their inventions or should the state grant them rights when they see fit?*”²⁹⁰ Robert Merges discusses that while European systems chiefly advocate the natural law perspective, the U.S. system generally supports the utilitarian view of intellectual property.²⁹¹ Peter Drahos argues that while natural rights-based “proprietaryism”²⁹² advocates moral supremacy of property fundamentalism and the capability of owning everything²⁹³, an instrumentalist view offers to undo the damage done by this view. However, he argues that both in the U.S. after the “anything under the sun that is made by man” doctrine propagated by the 1980 SCOTUS decision in *Diamond v Chakrabarty*²⁹⁴, and in Europe by eventually extending the patentable subject matter protection to isolated human genes, the natural theorist view is the dominant theory. However, it is important to note that this extension of the scope of granted rights to genetic inventions also derive support from the instrumentalist theories, namely the public benefit of advancing the health sector and developing new medicines, and the dependability of the biotechnology sector on patents for sustainability of their investments.²⁹⁵

²⁸⁹ Ibid.

²⁹⁰ Merges (n.279), p.94.

²⁹¹ Ibid.

²⁹² Drahos (n.279), p.200.

²⁹³ Ibid, p.201.

²⁹⁴ Ibid, p.210.

²⁹⁵ Pila (n.279), p.96.

For example, the language of the Biotech Directive is consistent with an instrumentalist view of intellectual property rights. Recital 46 of the Directive describes the function of a patent as “to reward the inventor for his creative efforts by granting an exclusive but time-bound right, and thereby encourage inventive activities.” Recital 11 provides that “ [...] the patent system should be [used] to encourage research in [the field of health].” As the instrumentalist views play a dominant role in the current legal framework, this suggests that the main task of patent offices when challenged with a new technology would be to assess the benefits against the costs of the patent and balancing the incentive and disincentives created by the grant.

In another example, Lord Neuberger states in the UK Supreme Court decision of *Human Genome Sciences Inc. v Eli Lilly*²⁹⁶ concerning patentability of a genetic sequence:

“[It] is worth remembering the purpose of the patent system, namely to provide a temporary monopoly as an incentive to innovation, while at the same time facilitating the early dissemination of any such innovation through an early application for a patent, and its subsequent publication. Although this is true in any sector, it has particular force in the pharmaceutical field, where even many of those who are sceptical about the value of intellectual property rights accept that there is a public interest in, and a commercial need for, patent protection.”²⁹⁷

Even though the patentability of genetic material may be justified for instrumentalist reasons, there is one more question that needs to be addressed that has been discussed ever since the biotechnological patenting has begun: *Are inventions concerning genetic material products of intellect, i.e. an invention?*²⁹⁸ As noted previously, intellectual property law, including patents, claims to protect the finer manifestations of human achievement –the products of the intellect – and this is the foundational principle of any proprietary right before it can be justified. While the issue is not completely resolved, there are some legal responses to the question posed above. We will now consider four judiciary responses²⁹⁸ and one statutory response.

In the 1969 German Federal Supreme Court case of *Red Dove*²⁹⁹, the court addressed the question of whether or not an invention concerning a biological method of selection and

²⁹⁶ [2011] UKSC 51, at [96]-[102].

²⁹⁷ Ibid at [99].

²⁹⁸ Pila (n.279), pp.101-105.

²⁹⁹ [1970] IIC 136.

breeding is a product of intellect or not. It applied the following test: in order for a natural force to become a patentable method, the method has to produce the exact same results in any number of trials it has been executed^{300,301}. Since then, the EPO applied the same test of technical teaching/effect in numerous cases. Consequently, the court's answer in this matter was that for the invention to be considered as a patentable intellectual product, it had to treat biological invention like any other mechanical method producing exactly the same product after each trial.

In the EPO case of *Howard Florey/Relaxin*³⁰² (henceforth *Howard Florey*) the EPO Opposition Division (henceforth OD) held that for the reason that the gene encoding for H2-relaxin had been “made available to the public for the first time”³⁰³, the invention concerning the genetic sequence was a product of the intellect.

In contrast with these two judicial responses, in *Brüstle v Greenpeace*³⁰⁴ (henceforth the *Brüstle* case), the European Court of Justice (henceforth ECJ)³⁰⁵ responded the question from a completely different point of view and advocated that the discussion of whether biological inventions are patent-eligible products of the intellect should not even be in issue because any proprietary right in such material would indicate economic interests in that material, and any part of human body should never be subjected to such treatment because it would violate the basic fundamental values and human dignity. Here the ECJ handled the biological matter not as chemical substances as indicated in *Red Dove* and *Howard Florey*, but as an extension of the human body.

Lastly, in the SCOTUS case of *Myriad (US)*, as discussed previously, it was held that merely isolated genetic sequences are products of nature and are not products of intellect, thus not capable of any sort of proprietary protection as it would be a form of unjust enrichment.³⁰⁶

Finally as a statutory response to the question, the Biotech Directive has taken a balanced stance of addressing the issue. According to Article 2(1) of the Biotech Directive, biological

³⁰⁰ Ibid, 138-140.

³⁰¹ Pila (n.279), p.102.

³⁰² [1995] EPOR 541

³⁰³ Ibid, 548.

³⁰⁴ C-34/10 [2012] CMLR 41.

³⁰⁵ The Court of Justice within the Court of Justice of the European Union (CJEU) will be referred to as the European Court of Justice (ECJ) in this paper for reasons of clarity.

³⁰⁶ Pila (n.279), p.105.

material is defined as “material containing genetic information and capable of reproducing itself or being reproduced in a biological system”. Article 3(1) of the Directive stipulates that biotechnological patenting involves inventions “even if they concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used” and as set forth in the following paragraph³⁰⁷ “biological material which is *isolated from its natural environment or produced by means of a technical process* may be the subject of an invention even if it previously occurred in nature” [*emphasis added*]. Therefore, according to the Directive what makes the biotechnological or genetic invention an intellectual product worthy of proprietary protection, even if it previously occurs in nature, is the involvement of any technical process executed by humans.

One last remaining issue to be addressed before moving on to the next section is “the triumph of moral reasoning”³⁰⁸ in the *Brüstle* decision. Under instrumentalist justifications for patentability of human biological material, including genetic sequences, the rationale is that for the behaviour to be encouraged there should be more benefits than harms to the society. In light of the ECJ’s reasoning in *Brüstle*, how would one reconcile the human dignity argument with an instrumentalist view? If commercialisation of human biological material were against human dignity, would this render the patentability of human biological material unjustified because eventually there would be more harms to the society than benefits, morally speaking? How would one fit a moral debate when assessing a cost-benefit type of analysis for the public?³⁰⁹ Although an inspection of possible approaches to these questions would be interesting, they remain outside the scope of this paper; it would suffice to acknowledge this side to the debate. After all, the debate of whether patent law should be free of a moral debate is a long and complicated one.^{310,311} According to some scholars³¹² the morality requirement under the EPC Article 53(a) and, later the Biotech Directive Article 6(1), should invite an assessment of European human rights law vis-à-vis the patentability of

³⁰⁷ Biotech Directive, Article 3(2).

³⁰⁸ J. Giles, ‘The *Brüstle* and *Eli Lilly* Cases: Creation –God or Humankind?’ (2012) 1 *Oxford Journal of Law and Religion* 518, p.512, cited in Pila (n.279), p.106.

³⁰⁹ See Deryck Beyleveld and Roger Brownsword, ‘Human Dignity, Human Rights and Human Genetics’ (1998) 61 *Modern Law Review* 661 for a more in depth analysis of the issue.

³¹⁰ See C. Cookson and others (eds), *Genetic Engineering: The New Challenge* (European Patent Office, 1993).

³¹¹ The issue was first raised in the case of *Howard Florey*, in light of Article 53(a) morality exception of the EPC, and it reached an era of intense debate especially following the case of *Harvard/Onco-mouse* T19/90 [1990] EPOR 501 where the EPO conducted a test evaluating the moral implications of the invention for the first time.

³¹² See Deryck Beyleveld and Roger Brownsword, *Mice, Morality and Patents: The Onco-Mouse Application and Article 53(a) of the European Patent Convention* (Common Law Institute of Intellectual Property, 1993); Geertrui Van Overwalle, ‘Gene Patents and Human Rights’ in Paul L.C. Torremans (ed), *Intellectual Property Law and Human Rights* (3rd edn Kluwer Law International, 2015), pp.871-915 for a more in depth analysis of the issue.

biotechnology as complementary principles because human rights law should define the limits of patent law in order for patent law to be recognised as “a tool fostering both private and public interest.”³¹³ With the Biotech Directive, which is part of EU law, patent law has finally invited fundamental rights into the discussion of patentability as seen in the ECJ decision in the *Brüstle* case. The Biotech Directive addresses the issue of human dignity with respect to patentability of human biological material in Recital 16:

“Whereas patent law must be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person; whereas it is important to assert the principle that the human body, at any stage in its formation or development, including germ cells, and the simple discovery of one of its elements or one of its products, including the sequence or partial sequence of a human gene, cannot be patented; whereas these principles are in line with the criteria of patentability proper to patent law, whereby a mere discovery cannot be patented.”

Although the extent of the morality exception and the test developed by the EPO over the years will be discussed later in the following sections, it is relevant, for the purposes of this section, to note here that an instrumentalist justification for human gene patenting also invites a moral debate of whether a gene patent should be assessed vis-à-vis human dignity.

IV. Substantive European Patent Law I: European Patent Convention

This section aims to explore the points where substantive patent law under the EPC falls short of addressing the issues specific to gene patents. After very briefly recounting the road to harmonization at the European level, the section will move on to the primary requirement of patentable subject matter and the morality exception; the secondary requirements of novelty, inventive step and susceptibility of industrial application; and the tertiary requirement of sufficiency of disclosure and the associated scope of protection. After problematic areas in all of these requirements are discussed, the next section will investigate how the overarching principle of industrial applicability under the Biotech Directive may address and resolve these problems in practice.

³¹³ Overwalle, ‘Gene Patents’ (n.312), p.885.

i) European Patent Convention 1973

The advent of international business and international trade called for a harmonised and centralised patent system in Europe.³¹⁴ The first attempt at harmonisation was through the Paris Convention for the Protection of Industrial Property of 1883.³¹⁵ As set forth by Article 2 of the Paris Convention, the signatory parties agreed to the criterion of “national treatment”, that is the application of same patentability principles reserved for the parties’ own citizens to the citizen of other states.³¹⁶ Pursuant to the establishment of the common European market with the creation of the European Economic Community in 1957, the second important attempt was the Strasbourg Convention in 1963.³¹⁷ The Convention, for the first time, introduced harmonisation of the substantive patent law principles at the European level. The Strasbourg Convention provided for the EPC³¹⁸ signed in 1973 in Munich and the establishment of the EPO. As the EPC aims to harmonise the substantive patent laws of the signatory parties, the EPO offers an easier and centralised way to obtain a bundle of national patents in designated contracting states.³¹⁹

As mentioned before, under the EPC, patentability of an invention is assessed under a three-tiered test of requirements. Lets now move on to a discussion of each requirement with respect to patentability of genetic inventions.

ii) Primary Patentability Requirement: Patentable Subject Matter

Article 52 of the EPC sets forth the requirement for patentability as:

³¹⁴ Stazi (n.65), p.178.

³¹⁵ Paris Convention is administered by the World Intellectual Property Organisation (WIPO) and it is the first international convention covering industrial property including patents, utility models, industrial designs, trade marks etc. It was signed on 20 March 1883 and later amended in 1900, 1911, 1925, 1934, 1958, 1967 and lastly in 1979.

³¹⁶ Stazi (n.65), p.179.

³¹⁷ “Convention on the Unification of Certain Points of Substantive Law on Patents for Invention” (henceforth the Strasbourg Convention) was signed by the Member States of the European Council in Strasbourg on 27 November 1963.

³¹⁸ “Convention on the Grant of European Patents” was signed on 5 October 1973. In 2000, the EPC was extensively amended (EPC 2000) in order to modernise the European patent system in light of recent technological, political and legal developments and to bring the EPC into harmony with other international developments such as the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) of 1994 and the Patent Law Treaty (PLT) of 2000.

³¹⁹ Stazi (n.65), p.184.

“Patentable inventions

(1) European patents shall be granted for *any inventions, in all fields of technology*, provided that they are *new, involve an inventive step and are susceptible of industrial application.*” [emphasis added]

What this article suggests that in order to be granted patent protection, an application must contain (1) a patent eligible invention; and if the subject matter meets this patent eligibility criterion, (2) patent worthiness of the invention, i.e. novelty, inventive step and industrial applicability, will be assessed. Article 52 continues:

“(2) The following in particular shall not be regarded as inventions within the meaning of paragraph 1:

- (a) *discoveries*, scientific theories and mathematical methods;
- (b) aesthetic creations;
- (c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers;
- (d) presentations of information.

(3) Paragraph 2 shall exclude the patentability of the subject-matter or activities referred to therein only to the extent to which a European patent application or European patent relates to such subject-matter or activities *as such.*”[emphasis added]

Accordingly, the fundamental patentability rule is that a patent is to be granted only for *inventions*. Therefore, in order to be patent-eligible an application should primarily contain an invention. However, the text of the EPC does not elaborate more on this. It does not provide for a definition of what an invention is, except for the list of patent ineligible inventions provided in Article 52(2) even if they are to be deemed patent worthy, i.e. fulfill the secondary requirement of novelty, inventive step, and industrial applicability. The Article gives examples of what is not an invention so it sets forth a negative definition of this elusive concept of an invention. Moreover, it is added in Article 52(3) that these patent ineligible inventions would not call for patent protection to the extent that an application involves them *as such*. So what is a patent eligible invention and what is not? What does “as such” suggest for the sake of formulating a test distinguishing between the two? Do the listed categories of

ineligible inventions have anything in common to present to the patentee regarding the formulation of a patentable invention?

It is important to note here that in the first codified text of a patentability statute, an invention was defined positively as “a manner of new *manufacture*.”³²⁰ Hence, in order to be consistent with the evolution of patent law, could a definition of patentable invention under the EPC, stem from the concept of “a manner of new manufacture”? Is it more sensible to think of an invention as a manufacture –something akin to the definition of patentable subject matter under U.S. patent law? The concept of manufacture is also linguistically more loaded with a higher importance given to the industrial applicability of a granted patent, which under the instrumentalist justifications makes sense. Even if an invention were to be defined broadly as an intellectual product as opposed to a product of nature, this too would be problematic because, as discussed in the previous section, it is debatable whether a biotechnological invention is essentially an intellectual product.³²¹

Additional to the discussion of what is a patentable invention, Article 53 of the EPC provides explicit restrictions for public policy considerations, regardless of whether or not the invention is both patent-eligible and patent-worthy:

“Exceptions to patentability

European patents shall not be granted in respect of:

(a) inventions the commercial exploitation of which would be *contrary to "ordre public" or morality*; such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States; [*emphasis added*]³²²

As with the concept of invention, the definitions and boundaries of the concepts of *ordre public* and morality (henceforth the morality exception) remain unclear.³²³ To sum up a patent

³²⁰ Statute of Monopolies of 1624, Section 6.

³²¹ Pila (n.279), p.155.

³²² Article 53 also restricts patentability of (b) plant or animal varieties and essentially biological processes for the production of plants or animals; and (c) methods of surgical, therapeutic, and diagnostic treatments. As the focus of this paper is patentability of genes, these exclusions remain outside the scope of this section and will not be discussed.

³²³ Pila (n.279), p.156.

examiner first asks the question of whether the subject matter of the application falls within the morality exception under Article 53 before moving on to the three-tiered requirements.³²⁴ Patent applications concerning biotechnological inventions³²⁵ have been highly contested under the morality exception under Article 53 and the requirement of an invention under Article 52 –i.e. the question of whether such products are products of human intellect (hence an invention) or products of nature (hence a discovery).³²⁶ As will be discussed later, the main legal response at the European level has been the enactment of the Biotech Directive in 1998, which ostensibly aimed to clarify the patentability criteria with respect to biotechnological inventions.³²⁷

In the following sections, first the evolution of the concept of an invention and a discussion of the intention of the parties of the EPC in drafting Article 52 will be addressed. This will be followed by an explanation of the “having a technical character” test that complements the negative definition of an invention under Article 52. Then, how the patent offices have worked with the morality exception under Article 53 will be explored. All these discussions of substantive law will be dealt with in relation to the patentability of biotechnological inventions and more specifically patentability of genetic material. The aim of the following subsection is to explore the ability of the EPC in addressing and resolving the issues related to the patentability of genetic material.

a. Requirement of an Invention

As Article 52(1) of the EPC confines patentability to “inventions, in all fields of technology”, the principle requirement of patentability is to have a patentable invention. This is fundamental for European patent law because the subject matter of every national patent law is the protection of an invention rather than a discovery. However, there is no commonly accepted clear distinction between a discovery and an invention in Europe. The text of the EPC only provides for a negative description via the inclusion of some apparent categories exemplifying what is not an invention, rather than a positive description of this

³²⁴ Ibid.

³²⁵ Products such as isolated DNA sequences that encode for proteins of pharmaceutical use, genetically modified plants more resistant to toxins, genetically modified animals used in medical research. Ibid.

³²⁶ Ibid, p.157.

³²⁷ Ibid.

requirement.³²⁸ The intention of the drafters was to elucidate the relationship between the industrial applicability and the invention.³²⁹ In the EPO Guidelines for Examination, this connection between what is an invention and susceptibility of industrial application is described as having ‘*a technical effect*’:

“If a new property of a known material or article is found out, that is mere discovery and unpatentable because discovery as such has *no technical effect* and it therefore not an invention within the meaning of Art. 52(1). If, however, that property is put to practical use, then this constitutes an invention which may be patentable. [To] find a previously unrecognized substance occurring in nature is also mere discovery and therefore unpatentable. However, if a substance found in nature can be shown to produce a technical effect, it may be patentable.”³³⁰

Accordingly, it can be stated that an invention must be technical, which have involved into the test of ‘technical effect’, which will be assessed later in this section. But before we conclude this part lets take a look at how the EPO defined ‘*technical*’.

In decision of the Technical Board of Appeal of the EPO (henceforth TBA) decision in the case of *IBM/Computer programs*³³¹ the concept of ‘technical’ was defined as having technical character, or providing a technical contribution. According to Bostyn in his background study to the European Commission³³², “this approach does not not really reveal the exact meaning of the concept of technical, since a definition of a term using the term to be defined in the definition cannot be a proper explanation of the term to be explained by that very definition.”³³³ Bostyn proposes that more emphasis should be put on defining the category of ‘a discovery’ rather than ‘an invention’:³³⁴ “A discovery, in other words, is the mere knowledge relative to something existing in nature, while invention implies the ability of a human being to use this knowledge in a technical way, the so-called ‘technical

³²⁸ EPC, Article 52(2) and (3).

³²⁹ Pila (n.279), p.172.

³³⁰ EPO, *Guidelines for Examination in the European Patent Office* (November 2016) Part G, Chapter II-2, at 3.1, section titled ‘Discoveries’ <<http://www.epo.org/law-practice/legal-texts/guidelines.html>> accessed 15 September 2017.

³³¹ T 1173/97 of 1 July 1998 [2000] EPOR 219 at 226-227.

³³² S.J.R. Bostyn, *Patenting DNA sequences (polynucleotides) and scope of protection in the European Union: an evaluation – Background study for the European Commission within the framework of the Expert Group on Biotechnological Inventions* (European Commission, 2004).

³³³ Ibid, p.12.

³³⁴ Ibid, p.14.

information’.”³³⁵ This approach is similar to the product of nature doctrine in the U.S. patent law and additionally, it is important to notice that the Biotech Directive adopted a similar positive description of an invention with regards to biological matter, as set forth in Article 3(2) as “biological matter that is isolated from its own environment or is produced through technical process may be the subject of invention, even if existed previously in its natural state.”³³⁶

A common ground for the list of exceptions?

The categories of excluded subject matter caused problems for the patent officials because they had difficulties in finding a common ground for drawing conclusions from the list. The negative test of Article 52(2) and (3) of the EPC evolved to be a confusing rule especially when examining the patentability of the inventions related to new complex technologies. As these categories seem arbitrary and for policy considerations³³⁷, Article 52(2) and (3) of the EPC faced with a lot of criticism at national courts. For example in the U.K., the Court of Appeal of England and Wales case of *Aerotel Ltd v Telco Holdings Ltd*³³⁸, Lord Justice Jacob explained his doubts regarding to the approach of the EPC:

“The categories are there but there is nothing to tell you one way or the other whether they should be read widely or narrowly. [...] Some categories are given protection by other intellectual property laws. [...] some categories are so abstract that they are unnecessary or meaningless. For instance, [how] would a scientific theory ever be the subject of a patent claim in the first place? Einstein’s special theory of relativity was new and non-obvious but it was inherently incapable of being patented. [...] There is or may be an overlap between some of the exclusions themselves and between them [...] and the overall requirement that an invention be ‘susceptible of industrial application’. The overall requirement is, perhaps surprisingly, hardly ever mentioned in the debate about the categories of ‘non-invention’ but it is clearly a factor lying behind some of the debate. [...] So one can at least confirm that no overarching principle was intended.”³³⁹

³³⁵ Ibid.

³³⁶ Biotech Directive, Article 3(2).

³³⁷ *Aplin* (n.242), p.577.

³³⁸ [2007] RPC 7.

³³⁹ Ibid at 126-127.

He also adds that according to the EU law tradition, exceptions are to be interpreted in a narrower sense.³⁴⁰ However, as the Article 52(2) categories are not explicitly stipulated as ‘exceptions to the patentability’, it is uncertain that whether this tradition applies to this article or not.³⁴¹

In another opinion, this time in a U.K. House of Lords case, obiter of Lord Hoffmann in *Biogen Inc v Medeva Plc*³⁴² stated that defining the requirement of invention with regards to more complex inventions which do not easily fit into the categories of excluded subject matter, judges should rely on assessing the secondary requirements of novelty, inventive step and industrial applicability rather than dismissing the invention based on intuition:

“Article 52 also has no definition of an invention. It seems that the parties to the EPC were unable to agree upon one. [...] But the reason why the parties were content to do without a definition was that they recognised that the question would almost invariably be academic. The four conditions [...] do a great deal more than restrict the class of “inventions” which may be patented. They probably also contain every element of the concept of an invention in ordinary speech. I say probably, because in the absence of a definition one cannot say with certainty that one might not come across something which satisfied all the conditions but could not be described as an invention. [...] As the four conditions are relatively familiar ground, elucidated by definitions in [...] the jurisprudence of the courts and the E.P.O., it will normally be more convenient to start by deciding whether they are satisfied. In virtually every case this will be the end of the inquiry. There may one day be a case in which it is necessary to decide whether something which satisfies the conditions can be called an invention, but that question can wait until it arises. One can of course imagine cases in which the alleged subject-matter is so obviously not an invention that it is tempting to take an axe to the problem by dismissing the claim without inquiring too closely into which of the conditions has not been satisfied. So in *Genentech Inc.'s Patent*

³⁴⁰ For example, this tradition of narrow interpretation can be observed in the *Harvard/Onco-mouse* cases. But it is important to note that that case involved Article 53 of the EPC, which is explicitly titled “Exceptions to patentability”.

³⁴¹ [2007] RPC 7 at para.12.

³⁴² [1997] RPC 1.

[1989] R.P.C. 147, 264 Mustill L.J. said, by reference to the ordinary speech meaning of “invention”: “You cannot invent water, although you certainly can invent ways in which it may be distilled or synthesised.” This is obviously right and in such a case it may seem pedantic to say that water fails [...] because it is not new. Unfortunately, most cases which come before the courts are more difficult. Judges would therefore be well advised to put on one side their intuitive sense of what constitutes an invention until they have considered the questions of novelty, inventiveness and so forth.”³⁴³

Justine Pila argues that it more reasonable to interpret the Article 52(2) and (3) in light of the intention of the drafters of the EPC.³⁴⁴ According to her, “while the exclusions are sufficiently diverse not to resolve to any positive definition or conception, such a conception can nonetheless be derived from the history and wider context of the EPC.”³⁴⁵ She claims that the main unresolved issue for the drafters of the EPC at the time was defining a clear relationship between inherent patentability and industrial/technical character and public policy on the text of the EPC.³⁴⁶ As this is the chief reason for the categories of excluded subject matter in the Article 52(2) and (3), she suggests a positive description of an invention: “The conception I have in mind requires a human action on the physical world producing an objectively discernible (material) result directed to advancing the industrial arts, where by ‘industrial arts’.”³⁴⁷

Now lets move on to how the EPO case law dealt with the problem of defining an invention.

Technical character test

In order to respond to the problems associated with the negative description of an invention, as mentioned before, the EPO case law established the positive requirement of a ‘technical character’ or ‘technical subject matter’ test. Therefore, instead of asking if the subject matter of the application belongs to one of the unpatentable categories, the EPO will ask if the

³⁴³ Obiter of Lord Hoffmann in *Biogen Inc v Medeva Plc* [1997] RPC 1, at 41-42.

³⁴⁴ Justine Pila, ‘On the European Requirement for an Invention’ (2010) 41(8) IIC 906.

³⁴⁵ Ibid, p.913.

³⁴⁶ Ibid.

³⁴⁷ Ibid, p.914.

application has ‘technical character’.³⁴⁸ Even if a subject matter has a single technical feature, which is not necessarily a dominant technical feature, then that subject matter will be deemed as an invention for the purposes of the EPC.³⁴⁹ However, having ‘a technical character’ does not imply that the invention is making ‘a technical contribution’. It is important to note here that, making a ‘technical contribution’ is not evaluated at this stage. As discussed in the TBA decision in *Vicom/Computer-Related Invention*³⁵⁰, the invention’s technical contribution will be evaluated when assessing novelty and inventive step.

The TBA summarises the principles governing the requirement of an invention in its decision in *Duns Licensing Associated/Estimating sales activity*³⁵¹, which is later affirmed by the Enlarged Board of Appeal (henceforth EBA) in the decision *President’s Reference/Computer program exclusion*³⁵²:

“[Having] technical character is an implicit requisite of an “invention” within the meaning of Art.52(1) EPC (requirement of “technicality”). Article 52(2) EPC does not exclude from patentability any subject matter or activity having technical character, even if it is related to the items listed in this provision since these items are only excluded “as such” (Art.52(3) EPC). [The] four requirements invention, novelty, inventive step, and susceptibility of industrial application are essentially separate and independent criteria of patentability, which may give rise to concurrent objections. [For] examining patentability of an invention in respect of a claim, the claim must be construed to determine the technical features of the invention, i.e. the features which contribute to the technical character of the invention. It is legitimate to have a mix of technical and “non-technical” features appearing in a claim, in which the non-technical features may even form a dominating part of the claimed subject matter. Novelty and inventive step, however, can be based only on technical features, which thus have to be clearly defined in the claim. Non-technical features, to the extent that they do not interact with the technical subject matter of the claim for solving a technical problem, i.e. non-technical features “as such”, do not provide a technical

³⁴⁸ Pila (n.279), p.173.

³⁴⁹ Ibid.

³⁵⁰ T208/84 [1987] EPOR 74 at 80-81.

³⁵¹ T154/04 [2007] EPOR 38.

³⁵² G3/09 [2009] EPOR 9.

contribution to the prior art and are thus ignored in assessing novelty and inventive step.”³⁵³

However, what the EPO means by the concept of ‘technical’ is only recently been explained by the EPC in the EBA decision in *Essentially Biological Processes*³⁵⁴:

“Human intervention, to bring about a result by utilising the forces of nature, pertains to the core of what an invention is understood to be. Like national laws, the EPC does not define the term “invention”, but the definition that was given many years ago in the “Red Dove” (Rote Taube) decision of the German Federal Court of Justice [...] set a standard which still holds good today and can be said to be in conformity with the concept of “invention” within the meaning of the EPC.

In that decision, in the version of the translation into English published in 1 IIC (1970), 136, the German Federal Court of Justice defined the term “invention” as requiring a technical teaching. The term technical teaching was characterised as “a teaching to methodically utilize controllable natural forces to achieve a causal, perceivable result.” [...]

The term “technology” (in German “Technik”), which is now enshrined in art.52(1) EPC but which at all material times underlay the understanding of the term “invention”, was deliberately not defined by the legislator in order not to preclude that adequate protection would be available for the results of developments in the future in fields of research which the legislator could not foresee. [...]

Ever since then, biological forces and phenomena, to the extent that they are controllable, have been considered to pertain to the area of technologies in which patentable inventions are possible [...]”³⁵⁵

[emphasis added]

Gene patents: discovery *as such* vs. invention?

So, when exactly does a scientific knowledge, an unpatentable discovery of a gene turn into a patentable technical invention? How does the patent law deal with this elusive

³⁵³ T154/04 [2007] EPOR 38 at 361.

³⁵⁴ G2/07 and G1/08 [2011] EPOR 27.

³⁵⁵ Ibid at [128]-[131].

transformation? Especially after the mapping of the human genome, providing an answer to these questions became essential for the sustainability of the existing patent law rules and concepts.³⁵⁶ The scientist who made the discovery will enjoy the fame, honours, and prizes. The industrialist, on the other hand, will enjoy the patent protection for the subsequent practical, i.e. ‘industrial’ applications of a discovery.³⁵⁷ Cornish and others explore some possible explanations for this dynamic, while noting that the reasons referred to remain unsatisfactory:³⁵⁸ A broad interpretation of an invention will commodify knowledge and will prevent free exchange of knowledge which is essential for the advance of technology³⁵⁹; basic knowledge may have multiple applications³⁶⁰; rewarding the first scientist who made the first discovery will confer him an unjust market lead with regards to the other applications waiting to be discovered³⁶¹.

Under Article 52 of the EPC, “discovery as such” is not a patentable invention. Gene patents were chiefly disputed under this article because it has been debated that whether an isolated gene would have technical character for the mere fact that it had been identified or identification is not enough to give the invention technical character because it still exists in nature as such, i.e. it is still a discovery. The TBA addressed these issues in the case of *Howard Florey*³⁶².

The claimed invention concerned a recombinant DNA sequence encoding for H2-Relaxin. H2-Relaxin is a naturally occurring hormone in the ovaries that is synthesized in order to relax the uterus during childbirth. Under Article 52(2)(a), the OD rejected the patent application on the grounds that it was an unpatentable discovery. However, upon appeal to the TBA, it was held that mere isolation of the gene, a substance naturally occurring in nature, would confer the invention enough technical character to deem it a patentable invention rather than an unpatentable discovery.³⁶³ On remand, the OD supported the TBA on the “the patentability of natural substances”³⁶⁴ that:

³⁵⁶ Cornish (n.213), p.897.

³⁵⁷ Ibid.

³⁵⁸ Ibid.

³⁵⁹ Ibid.

³⁶⁰ Ibid.

³⁶¹ Ibid.

³⁶² [1995] EPOR 541.

³⁶³ *Aplin* (n.242), p.603.

³⁶⁴ [1995] EPOR 541, at 548.

“[A] substance freely occurring in nature is mere discovery and therefore unpatentable. However, if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. *Moreover, if this substance can be properly characterized by its structure and it is new in the absolute sense of having no previously recognized existence, then the substance per se may be patentable.* [...] Human H2-relaxin had *no previously recognized existence*. The proprietor has developed a process for obtaining H2-relaxin and the DNA encoding it, has characterized these products by their chemical structure and has found a use for the protein. The products are therefore patentable under Article 52(2) EPC.”³⁶⁵ *[emphasis added]*

This decision demonstrated the practice of the EPO in applying the test of technical character to the genetic sequence patents. Isolation of a naturally occurring substance that has no previously recognized existence will provide the invention enough technical character to deem it sufficient to pass the primary patentability test of requirement of an invention, because it is no longer a discovery as such. But as set forth by the decision in *Howard Florey*, there are also policy considerations for deeming isolated genes patentable because the person who first made the gene available to the public deserves a proprietary protection over the gene.³⁶⁶ This decision and test has been reflected in the Biotech Directive Article 3(2)³⁶⁷ and Article 5³⁶⁸.

The discussion of where exactly genetic material falls in the context of the discovery versus invention debate seems to be resolved with the enactment of the Biotech Directive because Article 5(2) explicitly allows genetic sequences to be patentable subject matter. According to Article 5(2), an identification of the gene is a discovery until that gene is isolated from the body and transferred to an external environment.³⁶⁹ However, it is interesting to note that whether the SCOTUS decision of *Myriad (US)* will change the attitude in Europe towards patentability of genetic sequences remains to be seen.

³⁶⁵ Ibid.

³⁶⁶ Pila (n.279), p.175.

³⁶⁷ Article 3(2) stipulates: “Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature.”

³⁶⁸ Article 5 stipulates: “(1) The human body, at the various stages of its formation and development, and the simply discovery of one of its elements, including the sequence or partial sequence of a gene cannot constitute patentable inventions. (2) An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if that element is identical to that of a natural element.”

³⁶⁹ Stazi (n.65), p.210.

Furthermore, via the Article 3(1) the Biotech Directive resolved the debate by stating “the human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.” So, the involvement of a laboratory process when isolating the gene and producing the cDNA, which does not have to be inventive in itself, render it an invention.³⁷⁰ The Biotech Directive uses an overarching concept of “industrial applicability” while distinguishing this elusive gap between a discovery and an invention with regards to genetic inventions. When the difference is not obvious, what the Biotech Directive requires, which is also endorsed by the EPO, is to find “a immediate concrete benefit”³⁷¹ of the invention.³⁷² This overarching requirement of industrial applicability under the Biotech Directive, which addresses the problems raised by the lack of clear definitions under the EPC will be explored more in depth in the later sections. For now, let’s move on to the EPC’s treatment of the genetic inventions with regards to the morality exception.

b. The Morality and ‘*Ordre Public*’ Exceptions

The drafters of the EPC intended the concept of ‘*ordre public*’ to have a common European interpretation rather than having several varying national interpretations.³⁷³ For example, as stated by the TBA, in the case of *Plant Genetic Systems/Glutamine synthetase inhibitors*³⁷⁴ “the culture in question is the culture inherent in European society and civilisation.”³⁷⁵ Other than this, the drafters of the EPC provided for no further instruction on how to interpret the concepts of ‘*ordre public*’ and morality, and have not set forth clear margins on the meanings of these concepts.³⁷⁶ This work was left to the boards of the EPO and national courts. Over the years, the EPO developed three different assessments of the morality exception.

³⁷⁰ Cornish (n.213), p.899.

³⁷¹ *Tymogenetics/Haematopoietics cytokine receptor* [2007] EPOR 2.

³⁷² Cornish (n.213), p.900.

³⁷³ Pila (n.279), p.158.

³⁷⁴ T356/93 [1995] EPOR 357.

³⁷⁵ *Ibid*, at 366

³⁷⁶ Mills (n.218), p.53.

Assessing morality I: a balancing exercise of costs and benefits of the invention

The first time the EPO considered the extent of the morality exception was the utilitarian test conducted by the TBA in the case of *Harvard/Onco-mouse*³⁷⁷ (henceforth the *Onco-mouse* case) in 1990. This first test set forth by the EPO weighed the risks of the invention against the benefits of the invention to the public.³⁷⁸ The *Onco-mouse* patent filed on June 1985 claimed a method for producing a transgenic³⁷⁹ non-human mammal with increased susceptibility to developing cancer, and also claimed the animal itself. The Examining Division to the EPO (henceforth ED) at first did not refuse the application under the Article 53(a)³⁸⁰, and declared that the morality exception was irrelevant and patent law was not the appropriate tool for conducting a moral assessment of a patent application.^{381,382} However upon appeal, the TBA directed the ED to apply the morality exclusion: “The decision as to whether or not Article 53(a) EPC is a bar to patenting the present invention would seem to depend mainly on a careful weighing up of the suffering of animals and possible risks to the environment on the one hand, and the invention’s usefulness to mankind on the other.”³⁸³ This time, when the ED reevaluated the application, in the light of the TBA’s guidance on the morality exception, the patent was granted as the benefits of the invention outweighed the risks associated with it.³⁸⁴ According to the ED, “the invention’s usefulness to mankind cannot be denied. Cancer is one of the most frequent causes of death. Any contribution to the development of new and improved human anti-cancer treatment is therefore a benefit to mankind.”³⁸⁵ Moreover, “the use of the animals [gives] rise to a smaller number of animals being required when compared to the number of animals needed in corresponding conventional testing”³⁸⁶ and the invention

³⁷⁷ T19/90 [1990] EPOR 501.

³⁷⁸ Pila (n.279), p.159.

³⁷⁹ ‘Transgenic’ describes “an organism harbouring in its germ line a gene that has been introduced using cDNA technology[...]”. ‘Transgenic’ in Cammack (n.13).

³⁸⁰ The ED refused the application under the Article 53(b) animal variety exception, and argued that that exception should not be interpreted as restrictively as the plant variety exception because the plant variety exception exists in order to avoid double protection of plants under patent law and the *sui generis* plant breeder’s right established in the International Convention for the Protection of New Varieties of Plants 1961. For more on this issue, see the following EPO decisions: *Harvard/Onco-mouse* T19/90 [1990] EPOR 501; *Plant Genetic Systems/Glutamine synthetase inhibitors* T356/93 [1995] EPOR 357; *Novartis/Transgenic plant* G01/98 [2000] EPOR 303.

³⁸¹ [1990] EPOR 4, para.10.3.

³⁸² Aplin (n.242), p.616.

³⁸³ *Harvard/Onco-mouse* T19/90 [1990] EPOR 501, at 513.

³⁸⁴ *Harvard/Onco-mouse* [1991] EPOR 525.

³⁸⁵ *Ibid*, at 527.

³⁸⁶ *Ibid*.

would not pose any “possible risks to the environment [because the invention is] to be used exclusively in the laboratory under controlled conditions by qualified staff.”³⁸⁷

This case paved the way for the first time a moral analysis of the patent applications. Beyleveld and Brownsword discuss different approaches to the relationship between the Article 53(a) morality exception and the general patentability rules.³⁸⁸ They distinguish between three different approaches: (1) The facilitative approach; (2) the restrictive approach; and (3) a rational approach. Under the facilitative approach they argue that if “the Europe were issue a moral veto to applications, it will be deprived of the benefits of new technologies”³⁸⁹ and moreover over-regulation would leave Europe behind its competitors U.S. and Japan.³⁹⁰ Thus, the pro-patent lobby advocates flexibility of patent law vis-à-vis new technologies and calls for leaving any sort of moral veto outside the scope and predictability of patent law.³⁹¹ Under the restrictive approach, because the morality exception is part of the EPC³⁹², Article 53(a) requires an assessment of “the moral conception of patentability” rather than “a purely technical conception” of a patent.³⁹³ Lastly, as favoured by the authors, a rational approach would prefer an assessment of each patent application on its own merits so the assessment would neither automatically exclude an application claiming a biotechnological product nor automatically grant a patent because of the large sums of investment made in the research.³⁹⁴ Beyleveld and Brownsword also note that a purely utilitarian approach to morality would still create problems because of two reasons: (1) A cost-benefit analysis is based on assumed weights assigned to both sides of the arguments; and (2) such an approach does not necessarily recognize centrality of human rights³⁹⁵, which is central to an assessment of a European ‘*ordre public*’ and morality.³⁹⁶

³⁸⁷ Ibid, at 528.

³⁸⁸ Beyleveld (n.312).

³⁸⁹ Ibid, p.25.

³⁹⁰ For example, under the U.S. patent law, morality of the invention is not assessed and regulated by the patent office before the grant.

³⁹¹ Beyleveld (n.312), p.25.

³⁹² Ibid, p.38.

³⁹³ Ibid, pp.28,46.

³⁹⁴ Ibid, p.26.

³⁹⁵ Ibid, pp.57,70.

³⁹⁶ Ibid, p.118.

Assessing morality II: alternative approach

In the later EPO case of *Plant Genetic Systems/Glutamine synthetase inhibitors*³⁹⁷ in 1995, the TBA opted to rely on definition of concepts rather than conducting a cost-benefit analysis test adopted previously in the *Onco-mouse* case. Accordingly, the TBA has defined ‘*ordre public*’ as “the protection of public security and the physical integrity of individuals as part of society [...] encompassing also the protection of the environment [...] and inventions the exploitation of which is likely to breach public peace or social order or seriously to prejudice the environment.”³⁹⁸ Moreover, the TBA defined the concept of morality as “related to the belief that some behaviour is right and acceptable whereas other behaviour wrong, this belief being founded on the totality of the accepted norms which are deeply rooted in [...] the culture inherent in European society and civilisation.”³⁹⁹ According to this alternative approach of the TBA, the test is whether the invention deploys a subject matter conceived by the European cultural standards as outrageous and abhorrent.^{400,401} The TBA also stated that the morality exclusion to patentability should be interpreted restrictively in order to serve the intention of the drafters of the EPC, which is to maximize the scope of patentability, thus to maximize the number of patent grants which is thought to benefit the economic policy.⁴⁰² It is important to note here that these cases and the two different tests employed in assessing the invention in relation to Article 53(a) demonstrate that Article 53(a) might have not been helpful in determining restrictions on patentability on moral grounds as it has failed to establish legal certainty.⁴⁰³

Assessing morality III: inventions involving human biological material

It is important to note here two further points for a more complete overview of the morality exception. First point to note is that the discussion of the morality requirement also involves a discussion of donor consent when the invention concerns human biological material; however, as this subject provokes a separate debate on its own, the issue of consent will not be

³⁹⁷ T356/93 [1995] EPOR 357.

³⁹⁸ Ibid, at 366-7.

³⁹⁹ Ibid.

⁴⁰⁰ Pila (n.279), p.159.

⁴⁰¹ This test was first set forth in the earlier case of *Howard Florey*, which will be discussed in the next section.

⁴⁰² Pila (n.279), p.163.

⁴⁰³ Mills (n.218), p.74.

discussed for the purposes of this paper.⁴⁰⁴ The second point to note is that the morality requirement has also been incorporated into Article 6 of the Biotech Directive, which states that “inventions shall be considered unpatentable where their commercial exploitation would be contrary to *ordre public* or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.” Accordingly, the ECJ also proposed its own test of dignity in the *Brüstle* case⁴⁰⁵ in 2011, which to a certain extent confirmed the test adopted by the EBA in the case of *WARF/Thomsen stem cell application*⁴⁰⁶ in 2009. The test set forth by the ECJ is whether the commercialisation, i.e. patenting, of human biological material would offend fundamental rights of human dignity and human integrity.⁴⁰⁷ This view is also consistent with a combined reading of Recitals 39 and 43 of the Biotech Directive stating “ethical or moral principles supplement[ing] the standard legal examinations under patent law”⁴⁰⁸ should “respect fundamental rights, as guaranteed by the European Convention for the Protection of Human Rights and Fundamental Freedoms.”^{409,410} This test may refute any instrumentalist justification as it creates a rights-based⁴¹¹ examination for the patent application and would categorically deny any instrumentalist treatment of the human body.⁴¹² On the other hand, an instrumentalist justification may also integrate such an analysis as the protection of human rights, dignity and integrity may be considered to be a moral benefit to the society.

Concerning gene patents, the discussion of the morality assessment concerning human biological material made in the above paragraph raises the following question: would patents granted for isolated genes violate any fundamental rights as well? Unfortunately, as this issue

⁴⁰⁴ For more information of the issue see the relevant cases of *Howard Florey/Relaxin* [1995] EPOR 541; *Netherlands v European Parliament and Council of the European Union* C-377/98 [2001] ECR I-7079; *Breast and ovarian cancer/University of Utah* (T1213/05) of 27.9.2007 (Technical Board of Appeal); and the U.S. Supreme Court of California case *Moore v Regents of the University of California* 51 Cal. 3d 120 (1990). Additionally, note that according to the Recital 26 of the Biotech Directive “if an invention is based on biological material of human origin or if it uses such material, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent” for that invention to be deemed patentable. This is also consistent with the international principles of medical and research ethics such as Articles 6 and 7 of the UNESCO Declaration on Bioethics and Human Rights 2005. Pila (n.279), p.159.

⁴⁰⁵ C-34/10 [2012] CMLR 41.

⁴⁰⁶ G2/06 [2009] EPOR 15.

⁴⁰⁷ Pila (n.279), p.159.

⁴⁰⁸ Biotech Directive, Recital 39.

⁴⁰⁹ Biotech Directive, Recital 43.

⁴¹⁰ See Mills (n.218), pp.130-134.

⁴¹¹ See Beylerveld and Brownsword (n.309); and also see Brownsword’s conceptualisation of a “bioethical triangle” consisting of utilitarian, human rights and dignitarian perspectives as the main conflicting views in the morality debate concerning the regulation of biotechnology in Roger Brownsword, *Rights, Regulation, and the Technological Revolution* (OUP, 2008), pp.35-41.

⁴¹² Pila (n.279), p.161.

has not been addressed yet in a comprehensive manner by the ECJ or the EPO, and since the *Brüstle* test involved human embryos, which is an explicitly restricted subject-matter under Article 6(2) of the Biotech Directive, the answer to the question seems to be that there wouldn't be a violation. Although it may seem irrelevant at first look, in the U.K. case of *International Stem Cell Corporation v Comptroller General of Patents*⁴¹³, again concerning patentability of human stem cells, it was held that “the capability of commencing the process of development of a human being”⁴¹⁴ is not sufficient for the purposes of defining the human embryo, but “must necessarily have the inherent capacity of developing into a human being.”^{415,416} Although this decision concerns the definition of a human embryo, the relationship between the definition and the morality exclusion based on the human dignity test may illustrate how the Court may apply the same test to the gene patents; but as the genes by themselves do not have the inherent capacity to evolve into a human being, it is unlikely that human gene patents would fail the human dignity test applied in a similar way.^{417,418}

Assessing morality of gene patents

Finally, before we conclude this section, let's take a look at how the EPO assessed morality in the case of *Howard Florey*⁴¹⁹. Among other claims⁴²⁰, the patent was opposed chiefly because DNA represents ‘life’ and thus patenting ‘life’ would have been immoral.⁴²¹ Against this argument, the OD held that:

“[...] the allegation that human life is being patented is unfounded. It is worth pointing out that *DNA is not 'life', but a chemical substance which carries genetic information* and can be used as an intermediate in the production of proteins which may be medically useful. The patenting of a single human gene has nothing to do with the patenting of human life. Even if every gene in the human genome were cloned

⁴¹³ [2013] EWHC 807

⁴¹⁴ Ibid at [27].

⁴¹⁵ Ibid at [28].

⁴¹⁶ Pila (n.279), p.161.

⁴¹⁷ See the discussion in the following sub-section.

⁴¹⁸ Mills (n.218), p.135.

⁴¹⁹ [1995] EPOR 541.

⁴²⁰ For example, another important claim was that the patent application involved abuse of pregnant women and the issue of donor consent. Ibid, at 549.

⁴²¹ Pila (n.279), p.162.

(and possibly patented), *it would be impossible to reconstitute a human being from the sum of its genes.*^{422, 423} [*emphasis added*]

The OD also stated the importance of human proteins for medical purposes⁴²⁴, which illustrates the instrumentalist accounts for patentability of genetic inventions. And lastly, the OD provided a test for the general rule on the morality exception asking if “the invention is so abhorrent that the grant of patent rights would be inconceivable.”⁴²⁵ The OD recognized that “the EPO is not the right institution to decide on fundamental ethical questions”⁴²⁶ and stated that “[as] for the opponents' general assertions concerning the alleged intrinsic immorality of patenting human genes, these are founded on the premise that there is an overwhelming consensus among the Contracting States that the patenting of human genes is abhorrent and hence prohibited under Article 53(a). This assumption is false.”⁴²⁷ It is also important to note here that following the Biotech Directive, which explicitly states, “the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element”⁴²⁸ this approach regarding the patentability of genes most likely is still good law today. Article 5(2) of the Biotech Directive⁴²⁹ is later reaffirmed by the TBA decision of T272/95 *Relaxin/Howard Florey Institute* of 23 October 2002.

Next, we will discuss the problems in the secondary requirements of novelty, inventive step and industrial applicability of gene patents, which will prove to be problematic enough for patent law without the additional problem of the moral assessment of the genetic inventions.⁴³⁰

⁴²² [1995] EPOR 541, at 551.

⁴²³ This may suggest that even under the human dignity test of *Brüstle*, the gene patents would not be deemed violating any human right, dignity and integrity.

⁴²⁴ [1995] EPOR 541, at 551.

⁴²⁵ *Ibid.*, at 550.

⁴²⁶ *Ibid.*, at 552.

⁴²⁷ *Ibid.*

⁴²⁸ Biotech Directive, Article 5(2).

⁴²⁹ Which is added as the Implementing Rule 23(d) to the EPC.

⁴³⁰ Mills (n.218), p.105.

iii) Secondary Patentability Requirements: Novelty, Inventive Step and Industrial Application

a. Novelty

Patents are granted only if the claimed invention is new. According to EPC Article 54, “an invention shall be considered to be new if it does not form part of the state of the art.” The reasoning behind this requirement is to ensure that the patent is not going to prevent the public from doing what they have been doing before the grant of the patent, and also to justify the grant of the patent by ensuring that the proprietary right is conferred in exchange for new technical information made available to the public.⁴³¹ However, in order to defeat novelty, mere existence of prior information is not enough, the state of the art⁴³² must enable the person skilled in the art⁴³³ to anticipate the invention.⁴³⁴

Concerning genetic sequences, the identification and isolation of the gene from its outside environment will make it novel.⁴³⁵ This is the same principle applied to the novelty of chemical substances occurring in nature. According to this principle, even if a substance occurs naturally, when it is produced in a purer form, patent law can treat that substance as novel given that there are structural differences between the purer form and the natural form.⁴³⁶ With regards to genetic sequences, this principle applies even if the purer, i.e. isolated, gene sequence is structurally identical to its naturally occurring form. This divergence is explained by deriving novelty from the fact that the isolated gene, even if structurally identical to the naturally occurring molecule, makes the molecule available to the public for the first time. Accordingly in the TBA’s decision in *Pyridine herbicides/ICI*⁴³⁷, “a compound defined by its chemical structure can only be regarded as being disclosed in a particular document if it has been ‘made available to the public’ in the sense of Article 54(2) EPC.”⁴³⁸ Moreover, the fact that a DNA library⁴³⁹ contains the claimed DNA sequence would not defeat novelty because it has not yet been made available to the public.^{440,441}

⁴³¹ Aplin (n.242), p.647.

⁴³² For a detailed discussion of the concept of the ‘state of the art’ see *ibid*, pp.647-651.

⁴³³ The attributes of this hypothetical person skilled in the art are recounted in the U.K. Patents Court case of *Pfizer Ltd’s Patent* [2001] FSR 16 at [62]-[64].

⁴³⁴ Dianne Nicol, ‘On the Legality of Gene Patents’, (2005) 29 Melbourne University Law Review 809, p.822.

⁴³⁵ *Ibid*, p.831.

⁴³⁶ Bostyn (n.332), p.7.

⁴³⁷ T0206/83 [1986] EPOR 32.

⁴³⁸ *Ibid* at 236.

Lord Hoffmann in the U.K. House of Lords decision of *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd*⁴⁴² criticizes this practice of the EPO:

“The only case in which the EPO will accept a claim to a product defined in terms of its process of manufacture is when the product is new in the sense of being different from any existing product in the state of the art but the difference cannot be described in chemical or physical terms.⁴⁴³ [...] the requirement is that the product must be new and that a difference in the method of manufacturing an identical product does not make it new. It is only if the product is different but the difference cannot in practice be satisfactorily defined by reference to its composition, that a definition by process of manufacture is allowed. The latter may be a rule of practice but the proposition that an identical product made by a new process does not count as new is in my opinion a proposition of law. It cannot be new in law but not new for the purposes of the practice of the Office.”⁴⁴⁴

b. Inventive Step

Article 56 of the EPC provides that “an invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art.” While novelty assesses the state of the art quantitatively, inventive step analyses it qualitatively.⁴⁴⁵ The inventive step requirement ensures that the patents are granted only to inventions worthy of proprietary protection as opposed to inventions built on obvious adjustments of the state of the art.⁴⁴⁶ It also strikes a balance between the costs associated with restricting competition by assigning a monopoly to the patent holder and the benefits

⁴³⁹ A DNA library is “a collection of cloned DNA fragments representing the entire genetic material of an organism. (i.e. a genomic library) or just the genes transcribed in particular cells or tissues at a given time (i.e. a complementary DNA library, or cDNA library)...” ‘DNA library’ in Hine (n.133).

⁴⁴⁰ Bostyn (n.332), p.18.

⁴⁴¹ See the TBA’s decision in *Biogen/Recombinant DNA* T301/87 [1990] EPOR 190 at [5.1]-[5.3].

⁴⁴² [2005] RPC 9.

⁴⁴³ Ibid at 198.

⁴⁴⁴ Ibid at 199-200.

⁴⁴⁵ Aplin (n.242), p.685.

⁴⁴⁶ Ibid.

associated with the *quid pro quo* of the patent system.⁴⁴⁷ Thus, setting a right threshold for the test assessing the inventiveness of the invention is crucial for any patent system.⁴⁴⁸

The traditional test employed by the EPO is ‘the problem-solution approach test’⁴⁴⁹, which first establishes the closest state of the art and the technical effect achieved by that state of the art (‘the problem’), and then determines whether the technical effect of the claimed invention (‘solution’) was obvious⁴⁵⁰ in addressing that problem.⁴⁵¹ With regard to gene sequences, the EPO in the case of *Howard Florey* first employed a very broad test in assessing inventiveness, and held that the novelty of the genetic sequence was sufficient to demonstrate its inventiveness.⁴⁵² However, this approach is no longer valid.

The current test asks “whether the technique used to obtain the sequence information is ‘obvious’ to try.”⁴⁵³ An early guidance for this interpretation of inventiveness with regard to gene sequences can be seen in the U.K. Court of Appeal of England and Wales case of *Genentech Inc.’s Patent*⁴⁵⁴. There it was held that there was no inventive step in the discovery of the sequences because Genentech relied on the application of the known recombinant technology without any original step.⁴⁵⁵ In the context of the advent of a new and complex technology, it makes sense that every claim for an invention will seem dramatically new and inventive.⁴⁵⁶ However, in order for the patent system to promote and foster such complex technologies like genetic testing, the patent system must continue to treat the standard test of inventive step as meticulously as possible.⁴⁵⁷ It is important to note that the current technology used in DNA sequencing and isolation of a gene has become routine and heavily reliant on the computer power, which may question the inventiveness of the inventions concerning genetic sequences.⁴⁵⁸

⁴⁴⁷ Hazel V.J. Moir, ‘An inventive step for the patent system?’ (2013) 35 EIPR 125, p.125.

⁴⁴⁸ Ibid, pp.125-128.

⁴⁴⁹ See the EPO, *Guidelines* (n.330), Part G, Chapter VII-2, at 5, section titled “Problem-and-solution-approach”.

⁴⁵⁰ According to the EPO *Guidelines*, “the term “obvious” means that which does not go beyond the normal progress of technology but merely follows plainly or logically from the prior art, i.e. something which does not involve the exercise of any skill or ability beyond that to be expected of the person skilled in the art.” Ibid, Part G, Chapter VII-2, at 4, section titled “Obviousness”.

⁴⁵¹ Bostyn (n.332), p.19.

⁴⁵² Pila (n.279), p.192.

⁴⁵³ Nicol (n.434), p.832.

⁴⁵⁴ [1989] RPC 147.

⁴⁵⁵ Ibid at 155.

⁴⁵⁶ Cornish (n.213), p.908.

⁴⁵⁷ Ibid.

⁴⁵⁸ Nuffield Council on Bioethics, *Discussion Paper on the Ethics of Patenting DNA* (July 2012), p.29.

The EPO assesses the inventiveness of a gene patent not with regards to whether the sequence itself was obvious or not, but rather with regards to whether it is obvious to the person skilled in the art. The EPO states that: “*Prima facie*, the routine provision of further sequences having the same general function as the known prior art sequences of closely related structure is not inventive. The structural non-obviousness is not a reason to accept an inventive step; sequences as well as all other chemical compounds should solve a technical problem in a non-obvious manner to be recognized as inventive.”⁴⁵⁹ Accordingly, the current technology⁴⁶⁰ relying on the computer power in order to identify the gene sequences is unlikely to pass the inventive step of the EPO.⁴⁶¹

The Nuffield Council on Bioethics compares the low threshold of the U.S. ‘non-obviousness’ requirement with the firmer approach the EPO uses in its ‘inventive step’ test, suggesting that the test of the EPO as more appropriate.⁴⁶² It can also be argued that the higher threshold used in Europe may harm the European biotech industry in the long term.⁴⁶³ However, it is interesting to note that the current legal landscape is in the favour of the European biotech industry after the SCOTUS decision in *Myriad (US)*.

c. Industrial Application

Article 57 of the EPC stipulates “an invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture.” According to the EPO Guidelines, “‘industry’ should be understood in its broad sense as including any physical activity of ‘technical character’; [...] Article 57 excludes from patentability very few ‘inventions’, which are not already excluded by the list in Article 52(2).”⁴⁶⁴ It should be noted that, having industrial applicability is not a prerequisite overriding the test of technical character under Article 52(2).⁴⁶⁵ Two tests are patentability criteria that must be satisfied independently from one another. An invention having industrial application may not have technical character, and lack of technical character may not be

⁴⁵⁹ EPO, Japan Patent Office and USTPO, *Trilateral Project B3b, Comparative study on biotechnology patent practices – Theme: Patentability of DNA fragments* (November 2001).

⁴⁶⁰ Referred to as *in silico* approach, which means being performed on a computer or via a computer simulation (with reference to *in vivo* and *in vitro* methods used in biology and biomedicine).

⁴⁶¹ Nuffield Council (n.458), p.30.

⁴⁶² Ibid.

⁴⁶³ Cornish (n.213), p.909.

⁴⁶⁴ EPO, *Guidelines* (n.330), Part G, Chapter III-1, at 1, section titled ‘General Remarks’.

⁴⁶⁵ Bostyn (n.332), p.21.

objected under industrial applicability.⁴⁶⁶ The test of industrial applicability is for demonstration of some commercial value. If the claimed invention cannot be used in an industry, it would not have any commercial value, and thus it would not generate any public benefit in the long term.⁴⁶⁷ Under the instrumentalist account of a patent, this will render the invention not worthy of a proprietary protection because the inventor does not hold his end of the bargain. Until biotechnological patenting, this requirement was not a problematic issue in patent law.

The problem with the industrial applicability of genetic sequences is that the specific functions of a discovered DNA sequence are not always simultaneously discovered at the time of identification of the genetic data. It often takes more investment and research to uncover specific functions of the gene, so patent protection is often sought upon identification of the gene, before accruing the additional financial risk.⁴⁶⁸ Correspondingly, this situation causes problems concerning the interpretation of the test of industrial applicability. Is disclosing one *potential* function enough to satisfy the industrial applicability requirement?⁴⁶⁹ The answer to this question was in the affirmative since the grant of the first gene patents because as Article 57 prescribes, the claimed invention only needs to be *susceptible* of industrial application, which suggests that the invention should have the *potential* to be used in the market and generate commercial value.⁴⁷⁰ As this was the case, especially after the completion of the Human Genome Project, many gene patent applications were filed without demonstrating a sufficient and specific function, i.e. industrial applicability, of the sequence. The patentee only had to demonstrate the commercial capability of the invention, including its use for further research.⁴⁷¹ The issue of granting patents for such claims without specific function has since been controversial.⁴⁷² As a response to this problem, Margaret Llewellyn has suggested “a possible interim patent” that is granted for a limited time in order for the patent-holder to have more ‘protected’ time to demonstrate more specific commercial uses of the genetic sequence.⁴⁷³ However, courts have opted to interpret the industrial applicability requirement

⁴⁶⁶ Ibid.

⁴⁶⁷ Stazi (n.65), p.25.

⁴⁶⁸ Margaret Llewellyn, ‘Industrial Applicability/Utility and Genetic Engineering: Current Practices in Europe and the United States’ [1994] EIPR 473, p.474.

⁴⁶⁹ Stazi (n.65), p.25.

⁴⁷⁰ Bently (n.264), p.440.

⁴⁷¹ Llewellyn (n.468).

⁴⁷² Nuffield Council (n.458), p.31.

⁴⁷³ Llewellyn (n.468), p.480.

more restrictively in order to deal with the problems associated with its broader interpretation.

For example, in the U.K. Court of Appeal for England and Wales case of *Chiron Corporation v Murex Diagnostics Ltd*⁴⁷⁴, the patent claims on the polypeptides were held to be invalid because of lack of industrial application⁴⁷⁵: “[...] the invention can be made or used ‘in any kind of industry’ so as to be ‘capable’ of ‘susceptible of industrial application’. The connotation is that of trade or manufacture in its widest sense and whether or not for profit. But for industry does not exist in that sense to make or use that which is useless for any known purpose.”⁴⁷⁶ Trailing the USPTO Utility Examination Guidelines of 2001⁴⁷⁷, the OD of the EPO adopted a narrower interpretation of the industrial application requirement⁴⁷⁸ and held that “DNA sequences with indications of function which are not substantial, specific and credible shall not be patentable inventions.”⁴⁷⁹ The European Commission too affirmed the OD’s restrictive approach to the industrial applicability and stated that “the potential utilisation of a sequence disclosed in an application must not be speculative, i.e. it must be specific, substantial and credible.”⁴⁸⁰ And lastly, the Biotech Directive employs a similar approach as well, which will be discussed at length in the following section on the Biotech Directive.

iv) Tertiary Patentability Requirement: Sufficiency of the Disclosure

The scope of the patent protection is determined by the scope of the claims disclosed in the patent. Setting the third patentability requirement, Article 83 of the EPC stipulates: “The European patent application shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.” In biotechnology patenting,

⁴⁷⁴ [1996] RPC 535.

⁴⁷⁵ *Aplin* (n.242), p.628.

⁴⁷⁶ [1996] RPC 535, at 607.

⁴⁷⁷ Developments concerning the ‘utility’ criterion in the U.S. are discussed above in the section on U.S. patent law. According to the Guidelines, “an invention has a well-established utility (1) if a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (2) the utility is specific, substantial, and credible.” USPTO, *Utility Examination Guidelines* (January 5, 2001) 66(4) Federal Register 1092, at 1098 <<https://www.uspto.gov/sites/default/files/web/offices/com/sol/notices/utilexmguide.pdf>> accessed 17 September 2017.

⁴⁷⁸ *Icos Corporation/Seven transmembrane receptor* [2002] OJ EPO 293 (Opposition Division).

⁴⁷⁹ *Ibid* at [11(ii)].

⁴⁸⁰ Commission (EC), ‘Report from the Commission to the European Parliament and the Council - Development and implications of patent law in the field of biotechnology and genetic engineering’ COM/2002/0545 final at [52] <<http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52002DC0545>> accessed 17 September 2017.

lack of sufficiency has posed problems of granting excessively wide protection disproportionate to the disclosed claims. However, after the enactment of the Biotech Directive, with regards to gene patenting, this requirement has been dealt under Article 9 which provides that “the protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material [...] in which the genetic information is contained and performs its function” and Article 5(3) which states “the industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application.” The extent of these Articles will be discussed at length in the following section on the Biotech Directive.

V. Substantive European Patent Law II: The Biotech Directive

The objective of the Biotech Directive is to harmonise patent protection of biotechnological inventions “in order to *maintain and encourage investment* in the field of biotechnology”.⁴⁸¹ The European Commission first proposed a harmonisation directive in 1988, but the European Parliament vetoed the proposed directive in 1995 as a result of opposition based on the claim that the ethical questions concerning the patenting of biotechnological inventions were inadequately addressed.⁴⁸² Revising the proposal in the light of these objections, the Commission introduced a revised version in 1995, and finally in June 1998 the European Council of Ministers adopted the Biotech Directive. However, a few months after adoption, Netherlands brought an action for annulment before the ECJ in October 1998. The grounds for annulment were mainly procedural.⁴⁸³ In October 2001, the ECJ rejected the claims of the opposition.⁴⁸⁴ Some of the Directive’s provisions are incorporated into the EPC as Implementing Regulations; specifically, the EPC adopted the Directive’s approach to industrial applicability regarding genetic inventions.⁴⁸⁵ Although technically the EPC is not obliged to follow the Directive, but Implementing Rule 26(1) to the EPC stipulates that “Directive 98/44/EC of 6 July 1998 on the legal protection of biotechnological inventions shall be used as a supplementary means of interpretation.”

⁴⁸¹ Biotechnology Directive, Recital 3.

⁴⁸² D. Curley and A. Sharples, ‘Patenting Biotechnology in Europe: The Ethical Debate Moves On’ [2002] 24 EIPR 565.

⁴⁸³ A. Scott, ‘The Dutch Challenge to the Bio-Patenting Directive’ [1999] EIPR 212.

⁴⁸⁴ *Netherlands v European Parliament and Council of the European Union* Case C-377/98 [2001] ECR I-7079.

⁴⁸⁵ Pozo (n.106), p.42.

According to Pila and Torremans, the impact of the Directive has been fourfold⁴⁸⁶: (1) It granted the ECJ jurisdiction over the substantive patentability criteria and rules.⁴⁸⁷ (2) It put pressure on the EPO to act in harmony with the decisions of the ECJ in order to avoid any conflict and loss of legitimacy.⁴⁸⁸ (3) It exposed the patent law to fundamental values of human rights, dignity and integrity.^{489,490} (4) It codified the previously uncoded requirement for an invention with regards to the patentability of isolated genetic sequences.^{491,492}

Some of the principles and rules on the substantive patent law after the Biotech Directive have already been dealt in the previous sections. The following subsection will instead significantly focus on the overarching principle of industrial applicability and how this resurrected requirement addresses some of the problems associated with gene patents.

The Biotech Directive's approach to industrial applicability: an overarching requirement of industrial applicability?

The European Commission raised the threshold for the standard of industrial applicability and applied a stricter test for this requirement, thinking this to be the most appropriate response to the problems of granting gene patents for unspecific use.⁴⁹³ As a result, the usual principles governing the requirement of an industrial application have been extended.

The effects of this move can immediately be observed in the assessment of the primary patentability requirement of being a patentable invention. As set forth by the Recital 23 of the Directive, “a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention.” Therefore, in order to satisfy the technical character test distinguishing inventions from discoveries, a genetic sequence must have a function.⁴⁹⁴ Correspondingly, in Article 5(3) of the Directive, which is reproduced as the Implementing Rule 29(3) of the EPC, “the industrial application of a

⁴⁸⁶ Pila (n.279), p.177.

⁴⁸⁷ Ibid.

⁴⁸⁸ Ibid.

⁴⁸⁹ Ibid.

⁴⁹⁰ This has been discussed at length above, in section IV(ii)(b) “Assessing Morality III: Inventions Involving Human Biological Material”.

⁴⁹¹ Pila (n.279), p.177.

⁴⁹² This has been discussed at length above, in the section IV(ii)(a) “Gene Patents: Discovery *as such* vs. Invention?”.

⁴⁹³ Pozo (n.106), p.77.

⁴⁹⁴ Ibid, p.81.

sequence or a partial sequence of a gene must be disclosed in the patent application.” Before this new provision was introduced, the extent of industrial application did not give rise to any problems before the courts, and traditionally a broad interpretation of industrial applicability has been adopted by patent offices. Although how the Courts were going to deal with this new standard for the industrial applicability requirement was unclear, it appeared to be that Article 57 of the EPC and Article 5(3) of the Biotech Directive was not compatible.⁴⁹⁵ In 2000, a new interpretation for industrial applicability has been discussed in a Trilateral Project between Japanese, U.S., and European patent offices.⁴⁹⁶ They reached the conclusion that while a DNA sequence with no indicated specific function is not a patentable invention; a DNA sequence with disclosed specific function is a patentable invention.⁴⁹⁷

This new standard raised a lot of questions. First, as established by the decision of the OD in the case of *Icos Corporation/Seven transmembrane receptor*⁴⁹⁸, in order to establish industrial applicability, it was no longer enough to disclose that the claimed genetic invention could be made and used, but ‘a substantial, credible and specific’ use had to be disclosed at the time of the application.⁴⁹⁹ This new approach is far from the formulation of ‘making available for the first time’ made in the case of *Howard Florey. Icos Corporation/Seven transmembrane receptor* rendered this broad interpretation of industrial applicability obsolete. Later in the TBA decisions in *Multimeric Receptors/Salk Institute*⁵⁰⁰ and *BDP1 Phosphatase/Max Planck*⁵⁰¹, the EPO further distinguished mere research results from commercially exploitable genetic products. In both decisions the TBA emphasized the necessity to disclose a profitable use of the claimed invention.⁵⁰² In the later TBA decision in *Haematopoietic cytokine receptor/Zymogenetics*⁵⁰³, the meaning of ‘profitable use’ has been defined as having ‘an immediate concrete benefit’⁵⁰⁴ – the concrete benefit should be immediately obvious to the person skilled in the art, without requiring further research.

“[...] the need to show a “profitable use” is not to be understood in the narrow sense of an actual or potential economic profit (i.e. generating more income than

⁴⁹⁵ Ibid, p.87.

⁴⁹⁶ EPO, Japan Patent Office and USPTO, *Trilateral Project* (n.459) at Annex 2 p.43.

⁴⁹⁷ Pozo (n.106), pp.87-88.

⁴⁹⁸ [2002] OJ EPO 293 (Opposition Division)

⁴⁹⁹ Ibid.

⁵⁰⁰ T338/00 [2002] (Technical Board of Appeal).

⁵⁰¹ T0807/04 [2005] (Technical Board of Appeal).

⁵⁰² Pozo (n.106), p.93.

⁵⁰³ T0898 [2007] EPOR 2.

⁵⁰⁴ Ibid.

expenditure) or of a commercial interest (i.e. creating a new or increased business opportunity). Rather, it must be understood in the wider sense that the invention claimed must have such a sound and concrete technical basis that the skilled person can recognise that its contribution to the art could lead to practical exploitation in industry. It would be at odds with the purpose of the patent system to grant exclusive rights to prevent the commercial activities of others on the basis of a purely theoretical or speculative patent application. This would amount to granting a monopoly over an unexplored technical field.”⁵⁰⁵

Lastly, a more pro-industry approach⁵⁰⁶ to interpretation of industrial application has been adapted in the 2009 EPO⁵⁰⁷ and the 2011 UK Supreme Court (henceforth, UKSC)⁵⁰⁸ decisions of *Human Genome Sciences Inc. v Eli Lilly* (henceforth the *HGS (UK)* case and the *HGS (EPO)* case)⁵⁰⁹ This dispute concerned the validity of a patent claiming a human genetic sequence. The invention had two noteworthy features⁵¹⁰: (1) The gene was discovered by computer-assisted *in silico* techniques⁵¹¹; (2) the disclosed function of the protein encoded by the genetic sequence was based on the other similar proteins belonging to the same superfamily of proteins.⁵¹²

In *HGS (EPO)*, the TBA upheld the patent with more restricted claims because it held that the application disclosed a concrete technical basis. In *HGS (UK)*, Lord Neuberger rejected the earlier argument of Lord Justice Jacob in the Court of Appeal decision holding the patent invalid due to lack of any indication of specific use. Although, the Court of Appeal has applied the same principle as the TBA, Lord Justice Jacob applied the test more stringently and reached a different conclusion.⁵¹³ Lord Neuberger in the UKSC brought the standard of industrial applicability in the UK to the same level as the EPO. While the UKSC held that it was not enough to claim a sequence without a clear and specific practical use, it was noted

⁵⁰⁵ Ibid, at [14]-[15].

⁵⁰⁶ Lord Neuberger notes “it would be wrong to set the hurdle for patentability too high”: *Human Genome Sciences Inc. v Eli Lilly* [2011] UKSC 51 [120]; and Lord Walker added on the policy goal to “reduce the risk of a chilling effect in investment in bioscience”; Ibid at [171]. Additionally, Lord Neuberger acknowledges the policy considerations for favouring a pro-biotech industry interpretation of the industrial applicability requirement. Ibid at [96]-[102].

⁵⁰⁷ *Human Genome Sciences/Neutrokin*, T18/09 (21 October 2009, EPO Technical Board of Appeal).

⁵⁰⁸ [2011] UKSC 51.

⁵⁰⁹ Bently (n.264), p.441.

⁵¹⁰ Ibid, p.442.

⁵¹¹ Ibid.

⁵¹² Ibid.

⁵¹³ *Human Genome Sciences Inc v Eli Lilly & Co* [2010] RPC 14.

that “an educated guess”⁵¹⁴ would have been satisfactory to fulfil the industrial applicability requirement. The important question remains to be how to distinguish between ‘an acceptable educated guess’ and ‘purely speculative assumption’?⁵¹⁵ The answer depends on the type of evidence the Court is willing to accept.⁵¹⁶ In the *HGS (UK)*, while the lower courts demanded empirical data proving the claimed use of the invention, the UKSC was satisfied with plausible prediction, following the standard set by the TBA in the *HGS (EPO)*.⁵¹⁷

Timo Minssen and David Nilsson note that while it is evident from the decisions of the EPO that the current threshold for industrial applicability of a gene has been set higher, the *HGS* decisions bring more certainty to the regulatory framework of gene patenting.⁵¹⁸ On the contrary, Andrew Sharples argues that the UKSC has set a lower standard for the industrial applicability test for wider policy considerations.⁵¹⁹ He also suggests that the EPO too is far from setting a common standard for assessing the industrial applicability, and while the earlier cases insisted on an “immediate concrete benefit”, the *HGS (EPO)* ignored the “immediacy” and concluded only “a concrete benefit” would suffice, which is also supported by the *HGS (UK)*.⁵²⁰

And finally, the Biotech Directive uses the industrial applicability requirement in dealing with the problem of asymmetry between what is disclosed and what is protected. For example, it often occurred in practice that when a patent applicant claimed also the anticipated but unknown uses of the gene, the breadth of the protection would cover the anticipated but yet unknown commercial uses of the gene.⁵²¹ The scope of a patent has always been an important issue not only for lawyers but also for economics.⁵²² The breadth of the protection is important for the *quid pro quo* principle of patent law, and while a broad protection would facilitate the compensation of the costs of the inventor, a narrow protection would sustain

⁵¹⁴ Lord Neuberger provides for a 15-point summary of the EPO’s general approach to the principle of industrial applicability in *Human Genome Sciences Inc. v Eli Lilly*, [2011] UKSC 51 at [107]. At (viii) he states that “a “plausible” or “reasonably credible” claimed use, or an “educated guess”, can suffice.” Ibid.

⁵¹⁵ Bently (n.264), p.443.

⁵¹⁶ Ibid.

⁵¹⁷ [2011] UKSC 51, at [126].

⁵¹⁸ Timo Minssen and David Nilsson, ‘The Industrial Applicability Requirement for Biotech Inventions in Light of Recent EPO & UK Law: A Plausible Approach or a Mere ‘Hunting License’?’ (2012) 23 EIPR 698, pp.701-703.

⁵¹⁹ Andrew Sharples, ‘Industrial applicability, patents and the Supreme Court: *Human Genome Sciences Inc v Eli Lilly and Co*’ (2012) 34 EIPR 284.

⁵²⁰ Ibid, p.286.

⁵²¹ Nicol (n.434), p.835.

⁵²² Bostyn (n.332), pp.23-24.

competition even after the grant of the patent to the original invention.⁵²³ With the enactment of the Biotech Directive, currently the scope of gene patents is limited by way of Article 9 to “all material, [...] in which the product is incorporated and in which the genetic information is contained and performs its function.”⁵²⁴ As gene patents are protected to the extent that they demonstrate industrial applicability under Article 5(3), these two articles together limit the scope of patent protection to the disclosed commercial uses of the genetic sequences.⁵²⁵ Hence, the protection available to the genetic sequences is now “purpose-limited”.⁵²⁶ The ECJ confirmed this interpretation of Article 9 of the Directive in the case of *Monsanto Technology LLC v Cefetra BV et al*⁵²⁷. According to Pila and Torremans, this decision is important for the following two reasons⁵²⁸: (1) The scope of protection has been limited by reference to a patentability criterion⁵²⁹; (2) for the inventions concerning genetic sequences, the most important criterion of patentability is its claimed function, i.e. industrial applicability, because without any disclosed commercial use the patent ceases to exist.⁵³⁰

VI. Conclusion

Since the advent of new and complex technologies including biotechnology, there has been a lot of discussion regarding whether the existing patent law principles are able to accommodate inventions stemming from these technologies. Initial interaction between the substantive patentability requirements and the inventions concerning biological material, and more specifically genetic sequences, resulted in many problems as discussed in the above sections. A wide range of solutions have been suggested by many authors in the literature. For example, Marta Díaz Pozo helpfully lists various popular solutions dealing with these problems⁵³¹: “(i) The creation of a *sui generis* gene right; (ii) imposing stricter compulsory licensing for specific gene patents; (iii) raising the threshold for current substantive patentability requirements; and (iv) avoiding genetic patenting as a whole.”⁵³² With the enactment of the Biotech Directive, Europe seems to have opted for the third option of

⁵²³ Ibid, p.24; also see Pozo (n.106), Chapter 6.

⁵²⁴ Biotech Directive, Article 9.

⁵²⁵ Pila (n.279), p.203.

⁵²⁶ Ibid.

⁵²⁷ C-428/08 *Monsanto Technology LLC v Cefetra BV et al* [2010] ECR I-6765.

⁵²⁸ Pila (n.279), p.204.

⁵²⁹ Ibid.

⁵³⁰ Ibid.

⁵³¹ Pozo (n.106), p.76.

⁵³² Ibid.

raising the threshold of the current substantive patentability requirement under the overarching principle of a higher standard of industrial applicability.⁵³³

A stricter industrial applicability requirement safeguards the *quid pro quo* of the patent system so that patents are only granted for inventions providing real contributions to the society in the case of gene patents, and there is arguably less imbalance in the patent bargain.⁵³⁴ To a degree, this approach would also cooperate with the instrumentalist justification for patenting genetic sequences. A stricter industrial applicability requirement ensures patents are granted to patent-eligible and patent-worthy inventions, with protection proportionate to claims disclosed. The overarching industrial applicability requirement under the Biotech Directive offers a more balanced policy option addressing the issues concerning patentability of genetic sequences.⁵³⁵ Although this policy option does not provide an answer to every problem associated with gene patents, to large extent it prevents most of the negative effects of gene patents.⁵³⁶ Therefore, to sum up, it can be said that raising the threshold for current substantive patentability requirements is an efficient or at least more practical and feasible solution to the challenges gene patenting create.

We will now move on to the last part of this paper. First we will examine very briefly some of the alternative options other than increasing the threshold of substantive patentability requirements for inventions concerning genetic sequences, and then we will conclude by discussing some of the new CRISPR technology that could rise to further complications in the relationship between patent law and genetic inventions.

⁵³³ See *ibid* for a useful and more in-depth overview of this overarching industrial applicability requirement.

⁵³⁴ *Ibid*, p.226.

⁵³⁵ *Ibid*, p.229.

⁵³⁶ *Ibid*.

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D. OTHER OPTIONS, CRISPR, AND CONCLUSION

I. Alternative Options

The previous part analysed how the Biotech Directive increased the threshold for industrial applicability for patents claiming genetic sequences for preventing over-patenting in human genetics. Raising the threshold for substantive patentability requirements is only one of the various popular solutions addressing the problem of over-patenting. Although the Biotech Directive's approach to industrial applicability offers a balanced approach, as this new approach is not challenged enough before the ECJ, the limits of this solution is unclear the problems with gene patenting still is not completely resolved in the legal framework. Hence, before I conclude this paper, in order to offer a more complete overview of the issues, it is important to briefly introduce other solutions, namely widening the scope of experimental use exception and compulsory licensing, and a proposed *sui generis* gene right. However, it is important to note that, these topics are wide enough to develop into papers on their own. As they remain outside the main scope of this paper, which is the over-arching industrial applicability criterion under the Biotech Directive, it will be sufficient only to briefly introduce them.

i) Experimental Use Exception

In the justifications section, we have noted that under instrumentalist accounts for patenting, the *quid pro quo* principle is that the inventor discloses her invention to contribute to the common knowledge of the humankind, so nothing stays hidden and scientific and technological progress is facilitated. However, given the 20 year the proprietary protection, it creates a difficulty in experimentation by another scientist or inventor on the disclosed knowledge without infringing the patent.⁵³⁷ Cornish explains this tension as: "[...] if they [a person] may engage in such experiments as they please, the initial incentive of the patent may to a degree be diminished. But if they may not, the original patentee may control the further progress of a particular technology for the duration of his exclusive right."⁵³⁸ For this purpose, an 'experimental use' exception was introduced in Article 27(b) of the Community Patent

⁵³⁷ Aplin (n.242), pp.744-745.

⁵³⁸ W.R. Cornish, 'Experimental use of patented inventions in the EC states' (1998) 29 IIC 735.

Convention⁵³⁹ in 1989: “the rights conferred by a Community patent shall not extend to acts done for experimental purposes relating to the subject-matter of the patented invention.” It has been later adopted by national patent laws⁵⁴⁰ but so far the scope of this exception has not been harmonized. In the Advocate General opinion in the *Netherlands v European Parliament and Council of the European Union* case⁵⁴¹, Advocate General Jacob states that “experimental use is one such exception: experiments aimed at perfecting, improving or further developing inventions do not infringe the patent.”⁵⁴² Nuffield Council on Bioethics recommends that the scope of experimental use should be clarified in the U.S. and in Europe with regards to inventions concerning gene sequences.⁵⁴³

ii) Compulsory Licensing

The concept of compulsory licensing was introduced in Europe in the Paris Convention for the Protection of Industrial Property. Article 5(A)(2) sets forth compulsory licensing as “each country of the Union shall have the right to take legislative measures providing for the grant of compulsory licenses to prevent the abuses which might result from the exercise of the exclusive rights conferred by the patent, for example, failure to work.” In 1994, the concept was integrated as Article 31 to the Agreement on Trade Related Aspects of Intellectual Property Rights (henceforth, TRIPS Agreement). Under the TRIPS Agreement, compulsory licensing is when the government authorise commercial use of a patent to a third party, who can use the patent without the explicit authorization of the patent holder.

The scope of Article 31 has been discussed specifically with regards to pharmaceutical patents, as a reaction to the public health crisis in developing countries concerning high costs of pharmaceutical associated with patenting practice, the Doha Declaration on the TRIPS

⁵³⁹ Works on a European patent with unitary effect began in the 1970s. In 1975, the Luxembourg Conference on the Community Patent took place, and an intergovernmental treaty known as the Convention for the European Patent for the common market, or more commonly as the Community Patent Convention (CPC) was signed. Commission (EC) ‘Proposal for a Council Regulation on a Community Patent’ COM (2000) 412 final OJ C337E, 28 November 2000. It had the intention to create a single European Community patent, which would be obtained through a central procedure and would take effect on all Contracting Members. Nevertheless, the CPC was a failure because it was not ratified by enough countries and it never entered into force. Aplin (n.242), pp.555,558

⁵⁴⁰ For example, the U.K. section 60(5)(b) of the Patent Act 1977; the U.K. patent law case of *Monsanto Co v Stauffer Chemical Co* [1985] RPC 515; the German Supreme Court case of *Klinische Versuche I and II* [1997] RPC 623 and [1998] RPC 423; and for a comparison with the U.S. see *Maday v Duke University* 307 F.3d 1351 (Fed. Cir. 2002) and also Rimmer (n.141), pp.164-186.

⁵⁴¹ C-377/98 [2001] ECR I-7079.

⁵⁴² Advocate General Jacob’s opinion in C-377/98 at [27]

⁵⁴³ Nuffield Council (n.458), pp.71-73.

Agreement and Public Health was adopted by the World Trade Organization Ministerial Conference of 2001. The Doha Declaration was celebrated as a major breakthrough, encouraging developing countries to effective use of compulsory licensing mechanism under the TRIPS Agreement in order to address their public health problems.⁵⁴⁴ According to Matthew Rimmer, use of compulsory licensing for gene patents in Europe would help with the excess costs associated genetic diagnostic tests set by patent holders,⁵⁴⁵ so that compulsory licensing in genetic diagnostic testing would offer a balance between the “private interests of the patent holder” and “public interests”.⁵⁴⁶

iii) *Sui Generis* Gene Right

Some commentators argue that the patent system is fundamentally unsuited to be used for incentivizing investments in the biotechnology sector. The gist of this position is that the subject of genomic research and genetic engineering are natural phenomena and naturally occurring substances, which cannot and should not be considered as technical inventions, for which the patent system has been created.

For instance, according to Luigi Palombi, the broadening of the definition of (technical invention) for biotechnology 'products' is legally problematic as the international patent system by way of art. 27(1) of TRIPS presupposes a universal meaning for 'invention' as the preliminary requirement for patent eligibility.⁵⁴⁷ The same article prohibits discrimination between the various technical fields. According to this view, isolation of a polypeptide or a polynucleotide from their natural states (even if they are recombinant products) does not invest sufficient inventiveness in the biological product which categorically emulate the naturally occurring substance. Thus, any patentability criteria that recognize biotechnological products that are homologues of naturally occurring substances as inventions risk i)

⁵⁴⁴ Peter Rott, 'The Doha Declaration: Good news for public health' [2003] IPQ 284.

⁵⁴⁵ Rimmer (n.141), p.206.

⁵⁴⁶ For more information see: Esther Van Zimmeren and Geertrui Van Overwalle, 'A paper tiger? Compulsory license regimes for public health in Europe' (2011) 42 IIC 4.

⁵⁴⁷ Luigi Palombi, 'The Genetic Sequence Right: A *Sui Generis* Alternative to the Patenting of Biological Materials' in Johanna Gibson (ed), *Patenting Lives: Life Patents, Culture and Development* (Ashgate, 2008), pp.76-94. Art 27(1) TRIPS stipulates: “1. Subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. (5) Subject to paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced.”

contravening the meaning of 'invention' in art. 27 TRIPS, and/or ii) violating the prohibition of discrimination of technical fields in the same Article. According to Palombi, the EC Biotech Directive is guilty in both charges.⁵⁴⁸ Instead, Palombi argues for a 'Genetic Sequence Right' that will provide a 10 year right to a successful applicant for discovering the function and utility of a genetic sequence and disclosing the information related to the sequence, function and utility in a publicly available database. In exchange the genetic sequence right holder will have a right to a 'use fee' paid by parties that use the information in the database, the fee being calculated according to a preset tariff that will be sensitive to the nature of use; the right holder will have access to legal remedies against unlawful users of the information similar to remedies under patent law, however anyone who pays the use fee can use the information and use is not conditional on the authorization of the right holder.⁵⁴⁹

II. CRISPR and the Future

In the last four years, research in the gene editing method CRISPR⁵⁵⁰ (clustered regularly interspersed short palindromic repeat) has become the focal point of interest due to its enormous potential for genetic engineering applications but also the critical ethical implications of certain usages of the technology. CRISPR, in nature, is a defence mechanism that exists in various species of bacteria and nearly all species of archaeobacteria that uses short noncoding RNA molecules to splice and destroy invading viral DNA. To explain very basically, special proteins cleave a section of the incoming viral DNA, and integrate it in the bacterial genome in a section called the CRISPR locus. The CRISPR locus is then used for the transcription of polynucleotides called crRNAs that are complimentary to the sequence of the viral DNA from which it was originally taken. The crRNA are then complexed with special proteins called **Cas** proteins that attach to the associated viral DNA sequence should it invade again, and cleave the DNA, effectively destroying it. Thus, in case the bacterium or a part of it survives the initial viral infection, the bacterium or its descendants that carry the updated CRISPR locus will have gained a degree of immunity to future invasions of viruses

⁵⁴⁸ Palombi (n.547).

⁵⁴⁹ Ibid.

⁵⁵⁰ Jennifer A. Doudna and Emmanuelle Charpentier, 'The new frontier of genome engineering with CRISPR-Cas9' (2014) 346(6213) Science; Kurzgesagt – In a Nutshell, 'Genetic Engineering Will Change Everything Forever – CRISPR' (video: youtube.com, 10 August 2016) <<https://youtu.be/jAhjPd4uNFY>> accessed 10 September 2017.

that are represented in the CRISPR locus.⁵⁵¹ The bacterial CRISPR system is now being artificially used in other organisms to manipulate certain genes, and replicate the manipulations throughout successive generations of the species by making the changes in the genome inheritable, using a process called a gene drive.⁵⁵²

As with gene patents stemming from the advent of recombinant DNA technology, the inventions stemming from the CRISPR technology too may challenge the scope of the patentability requirements. Rimmer, for example, suggests that the rules and doctrines of substantive patent law should be tailored to the need of the specific technology.⁵⁵³ The CRISPR technology may allow manufacturing and designing human life in the near future. With this, we might witness a third period in the biotechnological inventions. As we have seen in the previous sections, as happened with the gene patents, the most efficient response would be increasing the thresholds of the existing patentability requirements. Additionally, as moral considerations are to an extent also part of the substantive patent law under the EPC and the Biotech Directive, a stricter application of the morality exception may also help in the problems that may arise with respect to inventions of CRISPR applications.

III. Conclusion

In the case of *Diamond v Chakrabarty* (1980), the Court avoided ‘the patentability of life’ objections to the claims covering bacteria, and developed its argument around the ‘product of nature’ doctrine. After all, a bacterium is on ‘the periphery of life’ and closer to non-living.⁵⁵⁴ Discussing gene patents as a matter of the patentability of life risk involving increasingly contorted arguments as more patent applications are made for highly complex biotechnological inventions that test our scientific and philosophical understanding of the definition of ‘life’. For example, Dr. George Pieczenik, a molecular biologist and a computer scientist, commented on his *amicus curiae* brief in the *Diamond v Chakrabarty* (1980) case that “[...] There is no single fundamental [...] principle which distinguishes that matter which we call living from that which we do not. To attempt to separate patentable from unpatentable

⁵⁵¹ Alberts, *Molecular Biology* (n.42), p.434.

⁵⁵² Michael Specter, ‘DNA Revolution’ [August 2016] National Geographic, p. 36.

⁵⁵³ Rimmer (n.141), p.299; also see Dan L. Burk and Mark A. Lemley, ‘Is Patent Law Technology Specific?’ (2002) 17 Berkeley Tech. L.J. 1155.

⁵⁵⁴ Rimmer (n.141), p.34.

subject matter on the basis of such a concept is to invite confusion in the art, to ignore the existing law and to ignore the scientific reality.”⁵⁵⁵

Yet, the basis of many biotechnological inventions is informational.⁵⁵⁶ The history of patent law portrays that it was traditionally designed to safeguard certain types of inventions.⁵⁵⁷ Then, patents were started to be granted to ‘the inventors’ of DNA sequences containing human genetic information.⁵⁵⁸ Should we consider a gene *a living matter, information carrier, or a chemical compound*? For example, in *Amgen v. Chugai*⁵⁵⁹, the Court defined a gene as “a chemical compound, albeit a complex one”. Rebecca Eisenberg discusses that there has been legal confusion on the degree of protection human genetic materials enjoy, and she argues three reasons for this legal confusion⁵⁶⁰: (1) Lack of clarity in the concept of gene; (2) rapidly developing new products –i.e. inventions, created by rapidly developing technology; (3) lack of clear responses from existing patent law because genetic inventions do not fit perfectly into the existing legal norms. Considering that even the science of biology is struggling with defining the concept of a gene and the information it contains, this struggle of patent law in its interaction with inventions concerning genetic material seems to be far from resolved.⁵⁶¹

The legal understanding of a gene stems from the understanding that one gene translates into one protein, and the patent system tries to work with this rather mechanical conceptualisation of a gene in order to patent genetic sequences.⁵⁶² For example, Eisenberg argues, “you cannot patent information, as such, that the subject matter of patents is limited to material products and processes and does not extend to knowledge and information about the world.”⁵⁶³ All the existing substantive patentability requirements are built on this estimated conceptualisation of a gene.

⁵⁵⁵ George Pieczenik, ‘Appellate brief of Dr. George Pieczenik as amicus curiae in support of the respondents in *Diamond v Chakrabarty*’, (1980 WL 339773, 29 January, 3-4), cited in Rimmer (n.141), p.37.

⁵⁵⁶ Mills (n.218), p.78; also see Judge Sweet’s opinion in *Association for Molecular Pathology v. USPTO* 702 F.Supp.2d 181 (S.D.N.Y. 2010).

⁵⁵⁷ Recall: The most emphasized reason was to provide economic incentives for technological and industrial progress in order to introduce new industries into national markets.

⁵⁵⁸ Hyo Y. Kang, ‘Processes of Individuation and Multiplicity: the Human Person in Patent Law relating to Human Genetic Material and Information’ (PhD thesis, European University Institute 2015), p.25

⁵⁵⁹ 927 F.2d 1200 (Fed. Cir. 1991).

⁵⁶⁰ Rebecca S. Eisenberg, ‘Re-examining the role of patents in appropriating value of DNA sequences’ (2000) 49(3) Emory L.J. 783, p.785.

⁵⁶¹ Kang (n.558), p.27.

⁵⁶² Ibid, p.29 *et seq.*

⁵⁶³ Rebecca S. Eisenberg, ‘Molecules vs. information: should patents protect both?’ (2002) 8 Boston University Journal of Science and Technology Law 190, p.195.

The aim of this paper was to explore the limits of substantive patent law in addressing gene patents, focusing specifically on how the EPC and the Biotech Directive has proposed to deal with the patentability of genetic sequences. In order to achieve this, this paper traced the evolution of the interpretations of the definitions of substantive patentability requirements of patentable subject matter, novelty, inventive step, industrial applicability and sufficiency of disclosure in the case law in the boards of the EPO and of the ECJ concerning inventions claiming genetic material.

Part A illustrated some of the issues surrounding personalised medicine applications and centrality of gene patents in protecting genetic diagnostic tests. Building on this, Part B introduced a historical account of the important developments in the relevant scientific and technological fields, and how U.S. patent law dealt with the new inventions concerning genetic material. The current legal framework in the U.S. now prevents the patentability of isolated genetic sequences following *Myriad (US)* and the patentability of ‘benchmarking’ type method claims on genetic risk assessment following *Mayo v. Prometheus*. Before moving on to the European response, demonstrating the current state of the art in the U.S. was important, because on a global level, harmonisation of the interpretations of substantive patent law is important for international trade. Hence, Part B concluded that following and *Mayo v. Prometheus* and *Myriad (US)*, it is uncertain how the EPC and ECJ will continue to interpret current legal framework with regards to patentability of genetic sequences.

Part C showed that the design of the European patent law was justified on instrumentalist accounts. For the early grants of gene patents, the patentability criteria were interpreted in a very broad way. However, this resulted in over-patenting and threats to health care provision. The enactment of the Biotech Directive addressed some of the concerns by raising the threshold of industrial applicability. With this new over-arching concept of industrial applicability, three major problems surrounding gene patents were efficiently resolved: (1) being a patentable invention as opposed to being a discovery *as such*; (2) granting patents with no designated commercial use, so falling short of the *quid pro quo* principle; and (3) granting patents with a scope too large and disproportionate to the claims. And finally, Part D briefly introduced alternative options (other than the overarching concept of industrial applicability) of a compulsory licensing, a broader experimental use exception, and a potential *sui generis* gene right. To conclude a brief account of the new CRISPR technology was given to illustrate the future of genetic patenting.

In light of all this, the paper concludes as follows: Although the gene patents are explicitly allowed in the Biotech Directive, the legal situation is far from certain following the decisions in *Mayo v. Prometheus* and *Myriad (US)*. However, fundamentally, the European substantive patent law under the EPC and the Biotech Directive, is better equipped to accommodate gene patents and with the raised threshold of industrial applicability, reasonably balances the public and private interests surrounding genetic patenting.

I wish to conclude this paper by acknowledging all people suffering from rare, complex and inheritable diseases, with the hope that developments in biomedical technology may provide them relief; and I call onto fellow lawyers to do our parts to ensure that they get it as quick and as affordably as possible.

Zeynep Timocin Cantekin
Florence, September 2017

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